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FIRST PERSON

First person – Sachiko Fujiwara

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. Sachiko Fujiwara is first author on 'Disease-associated keratin mutations reduce traction forces and compromise adhesion and collective migration', published in JCS. Sachiko conducted the research described in this article while a Postdoctoral fellow in Thomas M. Magin's lab at Institute of Biology, Division of Cell & Developmental Biology, Leipzig University, Germany. She is now an assistant professor in the lab of Kazunori Imaizumi at the Graduate School of Biomedical & Health Sciences, Hiroshima University, Japan, investigating the physiological roles of cytoskeletons.

Sachiko Fujiwara

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

The skin is predominantly composed of keratinocytes organized into a stratified epithelium that protects our body from chemical and mechanical stress. Basal skin keratinocytes are under tension at the ECM–cell interface and at cell–cell contact sites, which enables their adaptation to the environment through reorganization of their cytoskeletons through chemical and mechanical signals. The keratin intermediate filament provides structural support to epithelial cells and is linked to the ECM and to neighboring cells. Missense mutations in epidermal keratins K5 and K14 cause the severe skin blistering disease epidermolysis bullosa simplex (EBS) by compromising mechanical resilience, and outside-in and/or inside-out signal transduction in keratinocytes. However, the overall contribution of keratins to mechanotransduction and the underlying mechanisms remains unclear. In this paper, by comparing wild-type and EBS kerationocytes, we revealed that EBS keratinocytes with keratin aggregates showed reduced RhoA activity and generated lower traction forces, and displayed immature and redistributed focal adhesions. Our observations imply that defects in force sensing and mechanotransduction associated with keratin mutations contribute to EBS.

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

There were many impressive moments during the project, but the biggest one was when I discovered that cells with EBS-associated keratin mutations behave completely different from those lacking all keratins. Keratin-knockout cells strengthen their focal adhesions and exert high traction forces. In contrast, EBS keratinocytes with large keratin aggregates displayed disturbed focal adhesion distribution and developed lower traction forces. I was surprised, because in general, knockdown/knockout and expression of function-compromising mutants should yield the same results. Having repeated the experiment several times, I arrived at the conclusion that the EBS-associated keratin aggregates disturb the mechanotransduction machinery. It was a revelation to me that a mainstream concept is not always right.

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

The articles published in Journal of Cell Science are of high quality and reliable. The journal covers a wide range of cell biology, and I expect that JCS readers, with their diverse range of research interests, will be attracted to my manuscript.

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

Keratin intermediate filaments are important not only for providing structural support, but also regulate numerous cellular processes and represent a large protein family, which presents a big challenge for research into them. Fortunately, I was accepted to the lab of Prof. Thomas M. Magin, one of the leading intermediate filaments researchers. The discussions with him gave me many ideas, hypotheses, solutions, and stimulated me to succeed with my project. What I particularly liked was that he encouraged me to develop my own ideas and to try them out.

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?

Actually, I had left academia once after I graduated from my Masters degree, worked at a company for 5.5 years, and came back. I was a researcher in a drug discovery department of a pharmaceutical company. During that time, I was reminded of a lot of things we still don't know, down to processes in a single cell. Eventually, I realized that my interest was oriented to basic science, as I felt that revealing underlying molecular mechanisms of cellular events is essential for the medical progress of the future. My goal is to contribute to the understanding of disease mechanisms and development of molecular therapies by my research in fundamental cell biology.

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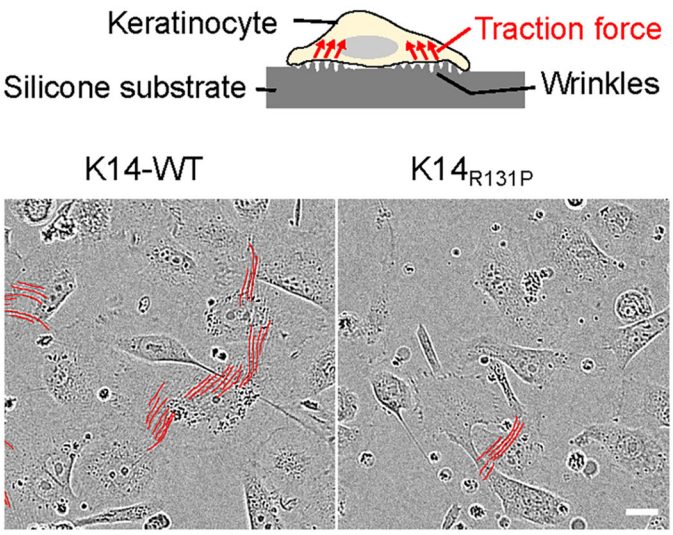

Cells expressing keratin with an aggresive EBS mutation (K14R131P) have a lower ability to exert traction forces, as visualized with a wrinkle assay. Wrinkles are shown by red lines. Scale bar: 20 µm.

What's next for you?

Having concluded my project with this paper, I have returned to my home country, Japan, to further my scientific career by joining a new lab working on cellular stress responses including mechanotransduction. Although the research field differs from my previous one, I continue to work on the cytoskeleton, which is fundamental to many cellular processes. My new work will clearly benefit from my previous knowledge and expertise in the function and regulation of cytoskeletal networks.

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

I like bird watching. I often take a walk at a park and look for birds with my binoculars on weekends. During my vacation, I enjoy traveling to places rich in nature where many birds live. I did the work for this paper in Leipzig, Germany, where I could see many birds that you wouldn't find in Japan. Watching birds gives me a change and calms me down even when I run into difficult problems in the research.

Reference

Fujiwara, S., Deguchi, S. and Magin, T. M. (2020). Disease-associated keratin mutations reduce traction forces and compromise adhesion and collective migration. *J. Cell Sci.* **133**, jcs243956. doi:10.1242/jcs.243956