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FIRST PERSON

First person – Yuki Yoshino

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. Yuki Yoshino is first author on 'RACK1 regulates centriole duplication through promoting the activation of polo-like kinase 1 by Aurora A', published in JCS. Yuki is an Assistant Professor in the lab of Natsuko Chiba at the Department of Cancer Biology, Institute of Aging, Development and Cancer, Tohoku University, Japan, investigating how BRCA1 dysfunction causes breast cancer.

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

Centrioles are important for normal cell division. Thus, centriole number is tightly regulated by coordinated duplication of centrioles in cell cycle. In previous research, we found that RACK1 is a new partner protein of BRCA1, which is a most frequent causal gene of hereditary breast cancer syndromes. RACK1 works with BRCA1 in the regulation of centriole duplication, but the molecular mechanism was not fully revealed. In this research, we found that RACK1 helps Aurora A to activate PLK1 by enhancing the binding between Aurora A and PLK1, which is an important regulator of centriole duplication. Previously, PLK1 was thought to be activated in late phases of cell cycle, G2 and M phase (the cell cycle is divided to G1, S, G2, and M phase, where M phase means the cell division phase). In this study, we revealed that RACK1 enhances PLK1 activation in S phase, before G2 and M phase, to support centriole duplication. Thus, our study suggests a new RACK1-mediated role of PLK1 in centriole duplication during S phase, where an importance of PLK1 activity was not known.

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

Both PLK1 and Aurora A are critical regulators of cell cycle. Thus, their inhibition disturbs the cell cycle and makes it difficult to analyze cellular events in relation to the cell cycle. We optimized the protocol for cell cycle synchronization and inhibitor treatment and contrived appropriate protocols.

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

We first obtained data indicating overexpression of RACK1 induced premature centriole disengagement by means of PLK1 activation, but the mechanism for how RACK1, which is not a kinase, could enhance phosphorylation of PLK1 was not understood. At that time, I recalled some papers reporting that RACK1 enhanced efficient formation of protein complexes by working as a scaffold. Then, I added RACK1 before immunoprecipitating Aurora A and PLK1 and found that RACK1 greatly enhanced the Aurora A–PLK1 interaction. This finding greatly accelerated our research.

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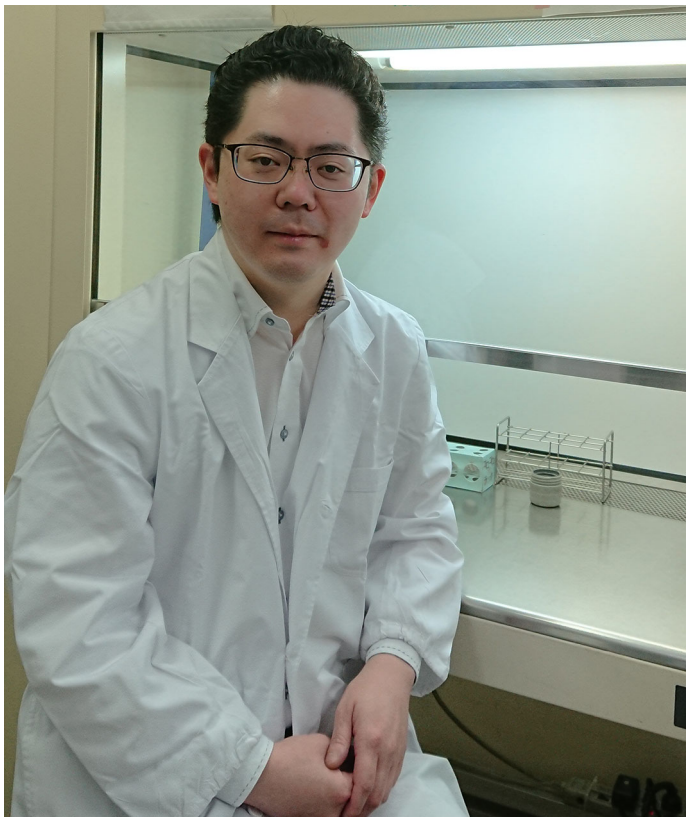

Yuki Yoshino

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

Our research was mainly based on cellular biology. Although we intended to reveal the molecular mechanism of carcinogenesis, the Aurora A–RACK1–PLK1 axis contributed to physiological centriole duplication. Therefore, we wanted to publish our research in a journal with broader interest than one specialized in cancer. Thus, we chose Journal of Cell Science.

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?

Besides being a researcher, I also work as a physician. When I was an undergraduate student of medicine, several molecular targeted drugs, such as EGFR inhibitors, PARP inhibitors and immune checkpoint inhibitors, had been developed and introduced in the clinical practice. These rapid developments of new therapeutics supported by basic science made me aim to become a physician–scientist.

Who are your role models in science? Why?

My role models are, for example, Dr Bert Vogelstein or Dr Vincent Theodore DeVita, Jr. because they are clinicians who are highly active in research.

What's next for you?

I will develop this research and other research seeds I have for the time being. Now, I am very interested in cancer prevention by means

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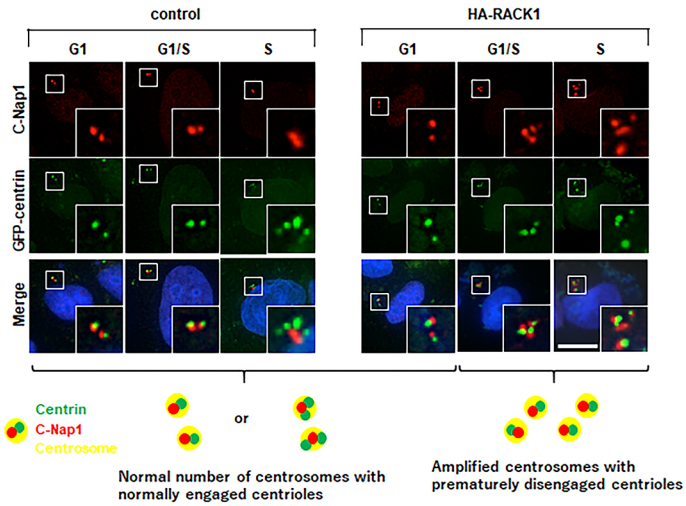

Excess RACK1 induces premature centriole disengagement in breast cancer cells, resulting in centrosome aberration.

of small molecules. If a certain signaling pathway (e.g. the Aurora A–RACK1–PLK1 axis in this research) is responsible for carcinogenesis mediated by BRCA1 dysfunction, manipulation of the signaling pathway will suppress breast cancer development. I am aiming to prove this hypothesis in future research. Someday, I want to improve clinical medicine, especially cancer treatment and prevention, with my research.

Reference

Yoshino, Y., Kobayashi, A., Qi, H., Endo, S., Fang, Z., Shindo, K., Kanazawa, R. and Chiba, N. (2020). RACK1 regulates centriole duplication through promoting the activation of polo-like kinase 1 by Aurora A. *J. Cell Sci.* **133**, jcs238931. doi:10.1242/jcs.238931