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FIRST PERSON

First person – Tomoaki Nagai

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. Tomoaki Nagai is the first author on 'Cullin-3–KCTD10-mediated CEP97 degradation promotes primary cilium formation', published in Journal of Cell Science. Tomoaki conducted the research in this article while an assistant professor in the laboratory of Prof. Kensaku Mizuno at Tohoku University, Sendai, Japan, investigating the mechanism of growth arrest-induced primary cilium formation. He is now a postdoctoral researcher in the laboratory of Dr Laurent Blanchoin and Dr Manuel Théry at the French Alternative Energies and Atomic Energy Commission (CEA) in Grenoble, France.

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

Our research interests focus on the understanding of primary cilia formation (ciliogenesis). Primary cilia are non-motile and serve as cellular antennae at the plasma membrane for sensing and transmitting a variety of chemical and mechanical signals. They thereby play essential roles in tissue development and homeostasis. Defects in primary cilium formation cause diverse human diseases, collectively termed ciliopathy, including polycystic kidney disease, retinal degeneration and neurodevelopmental disorders. Primary cilia are formed from the basal body, which is derived from the mother centriole of the centrosome. The centrosome plays important roles not only in ciliogenesis, but also in cell division. However, it cannot play these two roles at the same time and thus ciliogenesis generally occurs only when cells stop dividing. CEP97 and its binding partner CP110 are centrosomal proteins that cap the tip of the centriole to block ciliogenesis during cell division. Their removal from the mother centriole is one of the triggers for the onset of ciliogenesis. In this study, we analyzed the mechanism of removal of these proteins and found that CEP97 is degraded by the ubiquitin-proteasome system upon growth arrest signals and that CEP97 degradation promotes CP110 removal and ciliogenesis. We also showed the molecular players for growth arrest-induced CEP97 degradation. Our findings will contribute to better understanding of the molecular mechanisms of ciliogenesis and pathogenesis of ciliopathies.

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

The biggest challenge of this study was to determine the molecules responsible for CEP97 degradation. We first investigated several candidates that bind to CEP97 based on databases and its primary structure, but this approach was not successful. So we carried out focused siRNA-based screening and pharmacological experiments, and succeeded in determining that CUL3 was a strong candidate. Then, we successfully determined that KCTD10 is a strong candidate for mediation of CUL3-induced CEP97 degradation, thanks to the visible immunoprecipitation (VIP) assay and Human Proteome Expression Resource (HuPEX) clones.

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Tomoaki Nagai

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

We were surprised when we found that the proteasome inhibitor MG132 induced CEP97 ubiquitylation and formation of multiple CEP97 foci near the centrosome for the first time. These discoveries drove us forward to investigate the role of CEP97 ubiquitylation and degradation in ciliogenesis.

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

Journal of Cell Science has a good reputation in the field of cell biology, and thus we expect that our study will be broadly circulated through publishing in Journal of Cell Science.

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

I am most grateful to Dr Kensaku Mizuno for leading my scientific career since my undergraduate degree. He provides not only important ideas for my studies, but also taught me the basics of logical thinking and methods of developing my research. I also appreciate Dr Kazumasa Ohashi (Tohoku University, Sendai, Japan) for helpful advice and suggestions along my career development. I would like to take this opportunity to thank to Dr Tai Kiuchi (Kyoto University, Kyoto, Japan) and Dr Shuhei Chiba (Osaka City University, Osaka, Japan) for supervising me in the initial stage of my research career.

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 undergraduate studies, I was interested in molecular biology and biochemistry, but I was not sure how to broaden my

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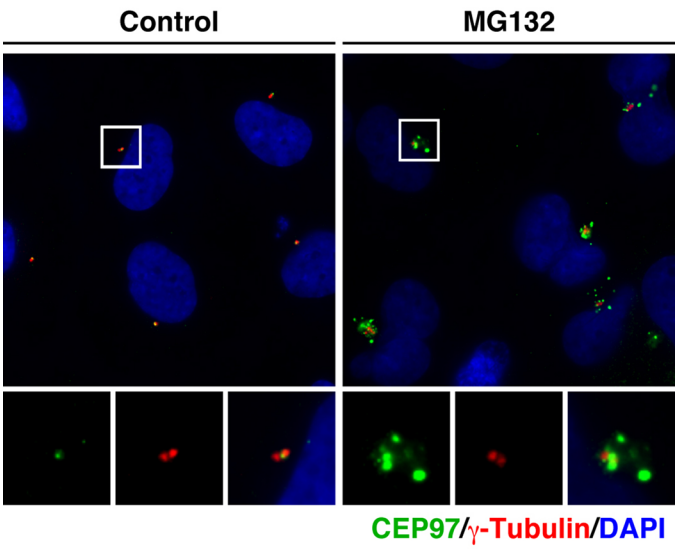

RPE1 cells were treated with 0.3 µM MG132 and analyzed by staining for CEP97 (green), γ-tubulin (red) and DAPI (blue). Bottom panels show magnified images of white boxes.

interest, and my path was not clear. I was fascinated with the biology of cell signal transduction, the cytoskeleton and its role in human diseases through Dr Mizuno's lectures, and I decided on a career as a cell biologist when I joined his lab. I will never forget these inspiring times.

What's next for you?

Recently I joined the laboratory of Dr Laurent Blanchoin and Dr Manuel Théry at the French Alternative Energies and Atomic Energy Commission (CEA) in Grenoble, France, as a postdoctoral researcher. I am working on the mechanisms of polarity establishment and centrosome positioning in epithelial cells.

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

I love spending time with my family. Since I moved to France on my own, I look forward to calling them once a week. I also like listening to pop music, running and cycling. In Grenoble, there are many places for hiking and skiing. I am looking forward to enjoying them.

Reference

Nagai, T., Mukoyama, S., Kagiwada, H., Goshima, N. and Mizuno, K. (2018). Cullin-3–KCTD10-mediated CEP97 degradation promotes primary cilium formation. *J. Cell Sci.* **131**, jcs219527.