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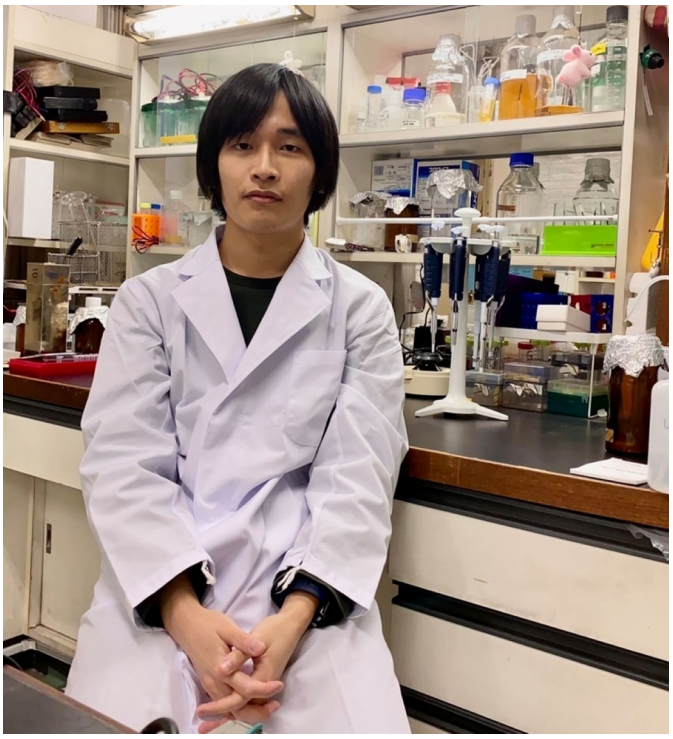
FIRST PERSON

First person – Akira Kawamura

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. Akira Kawamura is first author on 'DYRK2 maintains genome stability via neddylation of cullins in response to DNA damage', published in JCS. Akira is an undergraduate student in the lab of Kiyotsugu Yoshida at Department of Biochemistry, The Jikei University School of Medicine, Tokyo, Japan, investigating the function of dual-specificity tyrosine-regulated kinase 2, mainly in human cancers.



Akira Kawamura

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

DNA is constantly exposed to endogenous and exogenous factors, such as ultraviolet light, oxidative stress, carcinogens and radiation. To maintain genome stability, cells have cellular pathways collectively called the DNA damage response (DDR). Recently, abnormalities of the DDR have been found to induce genome instability, and this genome instability can cause carcinogenesis, neurodegenerative diseases and aging. Hence, clarifying the regulatory mechanisms of genome stability would provide insight into the pathology and development of new treatments of such diseases. In our current paper, we have shown that dual-specificity tyrosine-regulated kinase 2 (DYRK2) is a novel regulator of a cellular process called neddylation and maintains genome stability.

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

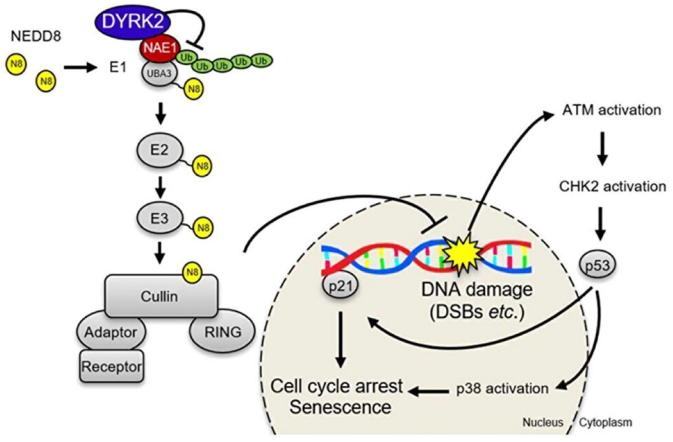
I started this research project in my second year of undergraduate school and devoted myself to this project for three years. At the same time, as a medical student, I spend much time at the hospital for clinical experience. It was very challenging for me to preserve enough time to do experiments. There was a time when I would do research all night without anybody else in the laboratory. I am very grateful for the assistance of my supervisor, Professor Kiyotsugu Yoshida, and Saishu Yoshida.

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

One of the 'eureka' moments was the first time I found that DYRK2 forms a complex with NAE1, which is a component of the NEDD8-activating E1 enzyme. It took a long time to clarify how DYRK2 regulates neddylation, and this finding provided me with a hypothesis into the unknown role of DYRK2.

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

Since I started my first research project in cell biology, I have frequently referred to Journal of Cell Science papers and I was keen to submit my first manuscript to JCS. Additionally, JCS is famous in cell biology, and so we felt our research would appeal to the researchers in related fields.



Schematic representation of function of DYRK2 in neddylation and DNA damage response. DYRK2 positively regulates neddylation through directly interacting with NAE1 and leading to inhibition of its ubiquitylation, which is needed for proteasomal degradation. In DYRK2-deletion cells, suppression of neddylation owing to the decreased protein levels of the NAE1-containing E1 enzyme causes dysfunction in DNA repair and accumulation of double-strand breaks (DSBs). The DSBs induce activation of p21 and p38 MAPKs via p53, and eventually lead to G0/1 phase cell cycle arrest and initiation of cellular senescence.

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What's next for you?

After graduation from college, I plan to work as a resident at the hospital for two years. In parallel, I would like to continue doing research in my current laboratory.

Many experiences encountered in clinical practice will provide me with tips about what is required in future basic research.

Reference

Kawamura, A., Yoshida, S., Aoki, K., Shimoyama, Y., Yamada, K. and Yoshida, K. (2022). DYRK2 maintains genome stability via neddylation of cullins in response to DNA damage. *J. Cell Sci.* **135**, jcs259514. doi:10.1242/jcs.259514