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FIRST PERSON

First person – Sung Tae Kim

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. Sung Tae Kim is the first author on 'The N-recognin UBR4 of the N-end rule pathway is targeted to and required for the biogenesis of the early endosome', published in Journal of Cell Science. Sung Tae Kim is a PhD student in the lab of Dr Yong Tae Kwon at University of Pittsburgh, Pittsburgh, USA, investigating the function of the N-end rule pathway in the ubiquitin-proteasome system and autophagy.

Sung Tae Kim

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

Just as people eat food and drink water, cells absorb various resources from the extracellular environment to maintain the energy supply and for cellular survival. Endocytosis imports extracellular cargoes through invagination of the plasma membrane to create vesicles. The primary endocytic vesicles containing external cargoes fuse with each other to form matured early endosomes in which the internalized cargoes are partially digested. We found that UBR4 deficiency suppresses the growth of early endosomes and leads to the disruption of endosomal processes, such as trafficking and proteolysis of internalized cargoes. This can be explained by cells suffering from 'indigestion' upon UBR4 deficiency.

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

Although we had no previous experience in computer-based screening, we tried to develop pharmaceutical inhibitors targeting UBR4 that prevented endosomal maturation. We did not know where to start but had a chance to access the DrugBank database (www.drugbank.ca) that is freely accessible and an online database containing bioinformatics and cheminformatics resource, combining detailed drug data with comprehensive drug target information. The database predicted that UBR4 can be targeted by picolinic acid. We further performed additional experiments to verify the interaction of picolinic acid with UBR4 via a pulldown assay. In the end, this enabled us to find a putative chemical to modulate the function of UBR4 in the early endosomal pathway. If you are interested in chemicals modulating your protein, I recommend you search these online-based databases first.

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

Although we observed the null phenotypes in UBR4-deficient animals and cells in which early endosomal maturation was suppressed, we were not able to explain how UBR4 works in the formation of the early endosome. The most important turning point was when we found references that reported that calmodulin bound to EEA1, an early endosomal component, and the correlation was required for early endosomal fusion. Although UBR4 had been identified as a calmodulin-binding protein, its functional relevance had remained unknown. In the end, we had a chance to explain the role of UBR4 in endosomal pathway. We hypothesized that UBR4 is associated with endocytic vesicles through the interaction with calmodulin. To validate the assumption, we performed *in vitro* interaction assays and immunocytochemistry analysis. The results showed that the association between UBR4 and calmodulin was important to maintain endosomal maturation. In my case, it was the reinterpretation of previous findings that was critical in our research.

"… it was the reinterpretation of previous findings that was critical in our research"

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

We have been focused on the N-end rule pathway in ubiquitin-proteasome system and autophagy. Therefore, we were beginners in the field of endosomal pathway. In preparation of this study, we had acquired lots of knowledge and techniques from original research papers published in Journal of Cell Science. Therefore, it was natural

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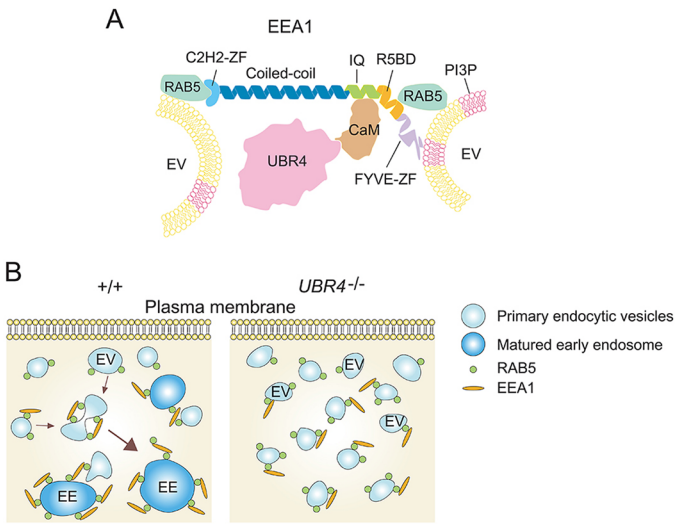

Schematic diagrams showing the role of UBR4 in early endosomal maturation. (A) UBR4 is recruited to endocytic vesicles through the interaction with calmodulin and facilitates early endosomal fusion. C2H2-ZF, Cys2-His2 zinc finger; CaM, calmodulin; FYVE-ZF, FYVE zinc finger; IQ, IQ calmodulin-binding motif; PI3P, phosphatidylinositol 3-phosphate; R5BD, RAB5-binding domain. (B) Schematic diagrams representing the dysregulated endosomal maturation caused by UBR4 deficiency.

for us to choose Journal of Cell Science. Additionally, my principal investigator Dr Kwon was also happy to submit to Journal of Cell Science due to its history and established reputation in the field.

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

I would like to express my deep gratitude to my mentor and academic advisor, Dr Yong Tae Kwon, whom I have had a great opportunity to work with. Since 2009, his faithful support has allowed me to pursue my research interests. He is a strong role model through his tireless passion for mentoring students. His enthusiasm and dedication to scientific research, which are transmitted to all lab members, have encouraged scientific discussion and fostered an excellent learning environment in our laboratory.

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?

Curiosity and fear are essential characteristics of a good scientist. As a child, I was unaware of the inevitability of death and what loss of the person who had loved me means until my mother was diagnosed with terminal cancer. At age 9, I didn't fully understand the implications of 'cancer', but my family's grimaces and tears made me aware, minimally, that it made people sad – although it would be some time before my mother's death awakened me to the disease's ultimate meaning. I grew up, appropriately, raising the larger questions of human disease and suffering. My mother's death left me focused on a career in the biological sciences.

"Curiosity and fear are essential characteristics of a good scientist"

Who are your role models in science? Why?

One of our collaborators is Dr Aaron Ciechanover who won the Nobel prize in chemistry in 2004 for his achievements in the ubiquitin-proteasome system. My group and he have had lots of small meetings to discuss scientific results and directions. I always have been impressed with his insightful suggestions and energetic passion. Additionally, he manages world-wide collaborations and is willing to participate in new scientific topics despite of his age. His eagerness and enthusiasm for scientific topics motivate me to be a great scientist.

What's next for you?

Recently, I have finished my PhD research and started looking for a postdoctoral position to pursue and advance my scientific ideas. And I am preparing a new paper relating to the cellular immune response that is not described in this article.

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

In my free time, I enjoy taking pictures with a film camera and develop black-and-white films myself. The oldest camera I have is a Contaflex alpha, which was produced by Zeiss Ikon in the 1950s. The vintage camera is still working and sometimes astonishes me with unexpected pictures. Ironically, my knowledge of analogue cameras helps me to understand the underlying principles of high-tech laser-scanning confocal microscopy.

Reference

Kim, S. T., Lee, Y. J., Tasaki, T., Mun, S., Hwang, J., Kang, M. J., Ganipisetti, S., Yi, E. C., Kim, B. Y. and Kwon, Y. T. (2018). The N-recognin UBR4 of the N-end rule pathway is targeted to and required for the biogenesis of the early endosome. *J. Cell Sci.* **131**, jcs.217646.