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FIRST PERSON

First person – Haymar Wint

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping researchers promote themselves alongside their papers. Haymar Wint is first author on 'Pacsin 2-dependent N-cadherin internalization regulates the migration behaviour of malignant cancer cells', published in JCS. Haymar conducted the research described in this article while an assistant lecturer at the Department of Biochemistry, University of Medicine 2, Yangon, Myanmar. She is now a PhD student at the Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University in the lab of Tetsuya Takeda and Kohji Takei at the Okayama University, Japan, investigating the molecular mechanisms of metastasis of cancer cells.

Haymar Wint

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

Metastasis is a hallmark of malignant cancer in which cancer cells move from the original tumor site to other places in the body. Cancer cells tend to migrate collectively during metastasis. However, molecular mechanisms underlying the collective migration of cancer cells remain unclear. Here, we identified the BAR domain protein pacsin 2 as a key regulator of collective cell migration in various types of cancer cells. Pacsin 2 directly binds to N-cadherin, an essential cell adhesion molecule, to regulate its internalization into cells (endocytosis). Depletion of pacsin 2 inhibits N-cadherin endocytosis, resulting in clusters of cancer cells that migrate in a collective and directional manner. Interestingly, pacsin 2 directly binds to N-cadherin, suggesting a key role in N-cadherin endocytosis to regulate the migration of cancer cells. Therefore, our study highlights pacsin 2 as a possible future therapeutic target to prevent collective cell migration in cancer metastasis.

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

Yes. In this study, we examined the role of pacsin 2 in N-cadherin endocytosis using a surface biotinylation and endocytosis assay. Optimization of this assay was quite challenging for me because the lab did not have any prior expertise. I overcame this challenge by working closely with my supervisor, Dr Takeda. We tested numerous conditions to establish the best protocol and succeeded in demonstrating that pacsin 2 is a key regulator of N-cadherin endocytosis.

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

Yes! At the beginning of the project, we aimed to explore the role of pacsin 2 in invasion of cancer cells. Unexpectedly, pacsin 2 depletion did not affect invasion per se but it induced clusters of cells that moved in a collective manner. Thus, we changed the direction of our research focus to unveil the role of pacsin 2 in collective cell migration. I remember the moment that I found the direct binding of pacsin 2 to N-cadherin in the GST pulldown assay. I was immensely happy as I noticed that my research was on the right track. Another moment that has stuck with me was when the live-cell imaging in the wound healing assay showed that pacsin 2 depletion caused directional movement of cancer cells. I was really excited about demonstrating the regulatory role of pacsin 2 in collective cell migration.

"I was immensely happy as I noticed that my research was on the right track."

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

JCS, being a well-established journal, has a longstanding reputation for maintaining exemplary research standards. Throughout my PhD studies, I have read numerous research articles published in JCS, from which I acquired substantial knowledge in cell biology. I deliberately selected JCS for publishing my research, as it fits within the aims and scope of the Journal to publish cutting-edge research in cell biology.

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

My PhD supervisor Dr Tetsuya Takeda gave me this great opportunity to work as a PhD student in his group, even though

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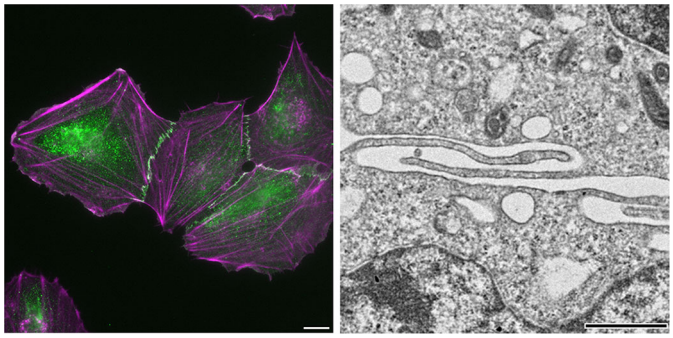

Pacsin 2 RNAi in T24 cells induces cell junctions enriched with N-cadherin. An immunofluorescence microscopic image of a cluster of pacsin 2-depleted cells stained for N-cadherin (green) and F-actin (magenta) (left), and an electron microscopic image of the junctional region between the clustering cells (right).

I didn't have much previous experience at bench work as I was previously a lecturer at a medical university in Myanmar. I have always been captivated by his distinctive and interdisciplinary approach to research. Additionally, I am also thankful to Professor Kohji Takei and other colleagues in the lab for their suggestions in lab meetings that helped to lead our work in the right direction. The main mentors in my life are my parents, who have nurtured me to grow into an independent and confident individual. When I made the decision to transition from being a medical doctor to a scientist, they had unwavering faith in my choice. My family has consistently provided me with psychological support, and they have been my biggest source of encouragement to continue pursuing this path.

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?

I think curiosity is the main thing that drives me to pursue a career in science. During my high school years, I found myself deeply engrossed in the world of science, constantly seeking new knowledges and discoveries from books. In medical school, I was intrigued by the significance of basic science in understanding disease mechanisms, which in turn have led to the discoveries of therapeutic interventions. This realization pushed me to pursue a career in science to explore the underlying mechanisms that are still poorly understood and develop better therapeutic options, especially in cancer.

Who are your role models in science? Why?

My PhD supervisor Dr Takeda has inspired me to pursue a career in cell biology and has provided me with guidance and support throughout my studies. One of the most significant aspects of his mentorship was his emphasis on critical thinking. He consistently challenged me to question assumptions, examine evidence rigorously and consider multiple perspectives before drawing conclusions. This approach not only improved the quality of my research, but also equipped me with essential analytical skills that have proven invaluable in my professional career as a scientist. I will follow his training when I supervise students in the future.

What's next for you?

Currently, I am in the last year of my PhD. After completing my thesis, I would like to stay in Japan to continue my postdoctoral training. After this, I will pursue a career in academia as a principal investigator.

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

I like cooking Burmese cuisine. This slightly relieved my homesickness and stress when I could not return to my home country because of the COVID pandemic, the military coup and the consequent brutal crackdown by the military in Myanmar.

How is life in Japan?

As my Japanese language skills are not very good, Google Translate has been the best companion for me during my stay in Japan. For academic discussions, however, I have no difficulties in communication with my PI in English. Outside of the lab, I enjoy my leisure time through many outdoor activities such as travelling and cycling. Hanami (cherry blossom viewing) was also very enjoyable!

Reference

Wint, H., Li, J., Abe, T., Yamada, H., Higaki, T., Nasu, Y., Watanabe, M., Takei, K. and Takeda, T. (2023). Pacsin 2-dependent N-cadherin internalization regulates the migration behaviour of malignant cancer cells. *J. Cell Sci.* **136**, jcs260827. doi:10.1242/jcs.260827