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FIRST PERSON

First person – Aini Gusmira

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. Aini Gusmira is first author on 'Regulation of caveolae through cholesterol-depletion-dependent tubulation mediated by PACSIN2', published in JCS. Aini conducted the research described in this article while a PhD Student in Shiro Suetsugu's lab at Nara Institute of Science and Technology, Ikoma, Nara, Japan. She is now an academic staff member in the lab of Dr Anton Bahtiar at the Faculty of Pharmacy, Universitas Indonesia, investigating the role of the cell membrane in disease processes.

Aini Gusmira

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

PACSIN2 (also known as syndapin II) is one of the membrane-deforming proteins that regulates cell membrane curvature for caveolae formation. The shaping of caveolae is not only affected by several specific proteins but also by particular lipids in the membrane. One of these lipids is cholesterol. Cholesterol is known to be essential for the formation of caveolae and interacts with various caveolar proteins. Previous studies have suggested that cholesterol-containing membranes bind strongly to structural proteins of the caveolar core, such as caveolin-1 (CAV1), caveolin-3 (CAV3) and cavin 1. PACSIN2 is also an essential protein for caveolae formation. In this study, we found that PACSIN2 has a weaker binding affinity for a cholesterol-containing model membrane than for a cholesterol-depleted model membrane. Interestingly, we found that PACSIN2 is not able to deform cholesterol-containing model membranes into a tubular shape. In the cell, the depletion of cholesterol causes disruption of the bulb-shaped caveolar structure, leading to the formation of a tubular structure mediated by PACSIN2. Therefore, we believe this study shows a novel mechanism of how PACSIN2 and cholesterol regulate caveolae formation.

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

Finding suitable lipid compositions for making liposomes as model membranes to study caveolae is time consuming. We tried several combinations of lipids and found that different lipids gave different results. None of these combinations showed satisfactory results at the beginning. The results seemed to be contrary to what would be expected from previous studies of the role of PACSIN2 in caveolae formation. After performing several experiments on liposomes prepared with various lipids, we revisited the literature regarding the lipid composition of caveolae and thought that a liposome composed of palmitoyloleoylphosphatidylcholine (POPC) and palmitoyloleoylphosphatidylserine (POPS) would be suitable for studying caveolae formation. This hypothesis was then tested in cholesterol-depleted cells. The result showed that when cholesterol was lacking, PACSIN2 changed the shape of caveolae from a bulb shape into a tubular structure, supporting the observation performed in POPC- and POPS-containing liposomes. PACSIN2 bound strongly to POPC- and POPS-containing liposomes and deformed these liposomes into a tubular shape. When cholesterol was included (a POPC-POPS-cholesterol liposome), the binding of PACSIN2 to this liposome was reduced and the formation of the tubular shape was diminished. Thus, we thought that POPC- and POPS-containing liposomes would be a suitable for model membrane to study caveolae.

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

Initially, none of the liposomes prepared with the various lipid compositions seemed to work and prove our hypothesis. Several experiments had been performed and many methods had been modified. When we found that cell experiments confirmed the results of the liposome experiments, we knew that our search had nearly come to an end, and that was when the 'eureka' moment happened.

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

Journal of Cell Science is a highly credible journal. Several caveolae-related studies conducted by reputable scientists have been published here, and thus this journal became one of our primary references.

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

I am really thankful to Prof. Shiro Suetsugu, my PhD supervisor, for the continuous support and guidance during this project. His great knowledge helped me during my research. He taught me how to see the bright side of missed opportunities and how to solve problems with limited resources. My sincere gratitude to my second supervisor, Dr Kyoko Hanawa-Suetsugu. She has always been open to discussing the results and taught me various methods in this area of research. My thanks also goes to Dr Kazuma Yasuhara, who

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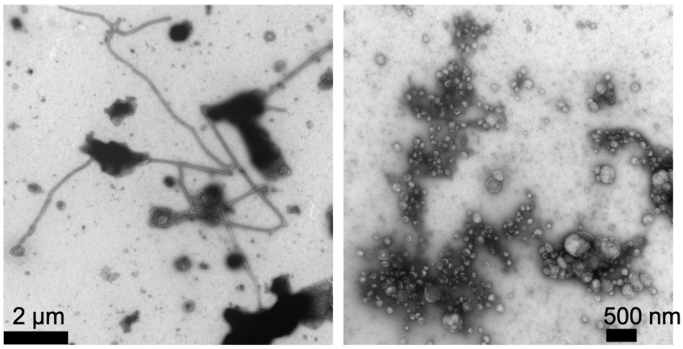

TEM images with negative stain showing liposomes remodeled by the PACSIN2 F-BAR domain. The PACSIN2 F-BAR domain deformed POPC-POPS liposomes without cholesterol into a tubular shape (left), whereas the POPC-POPS-cholesterol liposomes were not deformed into tubules (right).

taught me many things about liposomes, gave me access to his laboratory and research facilities and guided me during my work in his laboratory. Without my mentors' precious support, I would not have been able to conduct this research.

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 am a curious person and science makes sense of many parts of life. The more I know, the more questions come up. It is a never-ending process. When I studied molecular pharmacology during my master's degree, I found it interesting. Then, I had the opportunity to do research in this field. I enjoyed my work and I would love to do it again.

Who are your role models in science? Why?

I am impressed by Sir Alexander Fleming, who discovered penicillin in 1928, which led to the beginning the era of antibiotics. As we all know, antibiotics help to reduce the number of deaths by infection and became one of the greatest discoveries in therapeutic medicine. It was an accidental discovery. Upon his return from vacation, Alexander Fleming found his *Staphylococcus* culture plate was contaminated by mold. Instead of discarding the plate, he examined the mold and realized that it prevented staphylococci growth. That microbial contaminant was later known as penicillin. One lesson that I learned from this story is that, to become a good scientist, one needs to have sharp observation skill to imagine what would have happened.

What's next for you?

I finished my PhD a year ago and now I am working as an academic staff member at a university. I love doing research and I am looking for good research opportunities in molecular biology or pharmacology to sharpen my research skills.

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

I love swimming in crystal-clear rivers. I usually spend my free time watching movies or hanging out with friends.

Reference

Gusmira, A., Takemura, K., Lee, S. Y., Inaba, T., Hanawa-Suetsugu, K., Oono-Yakura, K., Yasuhara, K., Kitao, A. and Suetsugu, S. (2020). Regulation of caveolae through cholesterol-depletion-dependent tubulation mediated by PACSIN2. *J. Cell Sci.* **133**, jcs246785. doi:10.1242/jcs.246785