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FIRST PERSON

First person – Juri Luis Habicht, Ashley Mooneyham and Asumi Hoshino

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. Juri Luis Habicht, Ashley Mooneyham and Asumi Hoshino are co-first authors 'UNC-45a breaks the microtubule lattice independently of its effect on non-muscle myosin II', published in JCS. Juri Luis conducted the research described in this article while a research assistant in the lab of Martina Bazzaro at the University of Minnesota, USA. He is now a medical student in the lab of Prof. Dr Martin Heinze at Brandenburg Medical School Theodor Fontane, Neuruppin, Germany, investigating neuronal functioning and mental health. Ashley conducted the research described in this article while a graduate research assistant and PhD candidate with Martina Bazzaro. She is now a Director of Grants in the lab of Superior Medical Experts at St Paul, MN, USA and works on small business healthcare innovation. Asumi is a full-time researcher in the lab of Martina Bazzaro investigating the molecular basis of drug resistance in cancer.

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Juri Luis Habicht

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

J.H., A.M. and A.H.: Microtubules are tube-like structures that extend outwards from the center of a cell. They help maintain the cell's shape, like bones in a human body, when cells are not dividing. In a dividing cell, microtubules attach to the chromosomes (that contain the DNA) to pull them towards opposite poles. Cancer cells are rapidly dividing cells, thus microtubules and their associated proteins are good therapeutic targets to disrupt cell division and kill cancer cells. One commonly used anti-cancer drug, paclitaxel, stabilizes microtubules to inhibit their normal function in cell division, ultimately leading to cell death. Previous studies showed that paclitaxel-resistant human cancer cells have more UNC-45A (our protein of interest), and that this protein destabilizes microtubules to counteract the effect of paclitaxel. In this study, we demonstrated that UNC-45A binds to a microtubule, bends it and breaks it even when a microtubule is stabilized by paclitaxel. UNC-45A is shown to be associated with another protein (myosin II), which indirectly breaks microtubules. However, we demonstrated that UNC-45A breaks microtubules independently of myosin II. These findings are not only relevant for cancer research but may also represent important data for the research field of neurodegenerative diseases, like Alzheimer's disease (AD), as these diseases are connected to destabilized microtubules.

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

J.H., A.M. and A.H.: To show that UNC-45A bends and breaks microtubules in living cells, some of the techniques that we tried

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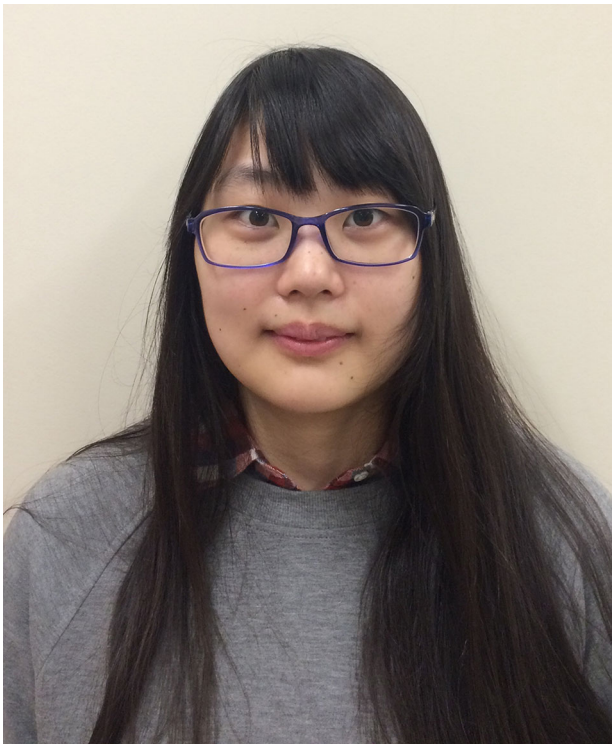
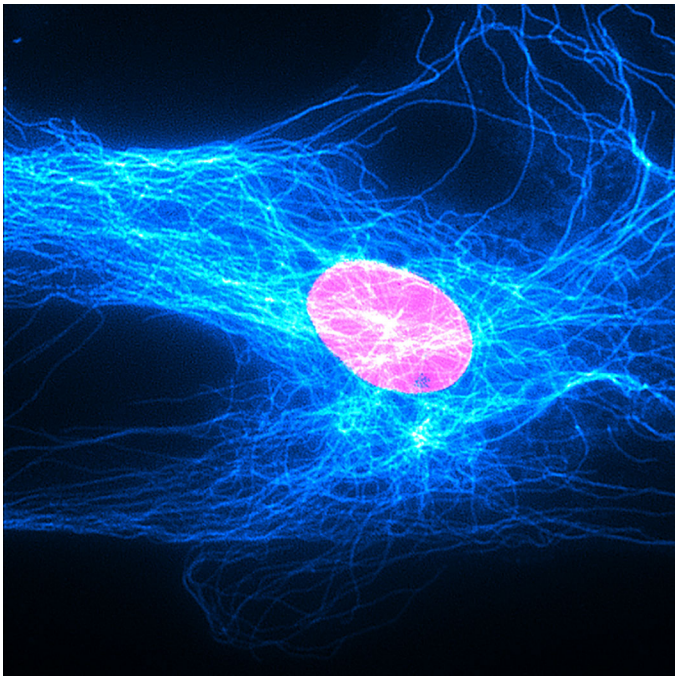


Asumi Hoshino



Visualization of microtubules in RFL-6 cell with fluorescence microscopy. The nucleus is colored in magenta. Microtubules are colored in blue.

(e.g. infection of cells with lentivirus plus using chemical 'infection' via Fugene to overexpress two proteins in a cell) were very challenging. Therefore, we used a taxol-based dye to label polymerized tubulins to see the effect of GFP-UNC-45A.

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

A.M.: The moment we discovered that N-teminally deleted UNC-45A was completely unable to bind to microtubules was very exciting, as it was our first tangible evidence toward which domain is required for UNC-45A's recently discovered microtubule-associated function.

A.H.: Since this is the first research project I've joined, seeing microtubule breakages in live-cell imaging in real-time was very interesting. It was fascinating to directly witness what cells were doing.

J.H.: Live-cell imaging was fascinating for me, too.

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

A.M.: We are very proud to have our work published in the Journal of Cell Science, signifying achievement of scientific excellence in the field of cell biology. The expert reviewers at JCS elevated our research, and we are thrilled to present our conclusions to the JCS readership and stimulate further conversation on microtubule-destabilizing proteins.

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

J.H.: I want to thank Ashley Mooneyham for her everlasting support and patience in the lab – no matter what day or time it was, she always helped me! And of course, I want to thank Dr Bazzaro for the chance to work in her team; it's been one of my greatest experiences as a medical student!

A.M.: Dr Bazzaro has been my most significant and inspiring mentor both inside and beyond the laboratory. She has an infectious enthusiasm for science and scientific discussion and her style of leading by example was very formative toward my scientific communication style.

A.H.: My PI, Dr Bazzaro, has been willing to help me to understand the concepts of scientific literature and laboratory techniques I performed, and gave me a lot of advice when I screwed up my experiments to figure out what went wrong ever since I joined her lab as an undergraduate student. I'm glad to be involved in her team.

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?

J.H.: I have always been fascinated by the human body, its millions of cells (and microtubules) and its (dis-)abilities. This awe has even been strengthened by the complexity that I was able to witness when I looked through the microscope to observe parts of a single cell. Watching the movement and interaction (or communication) between microtubules and other proteins makes the complexity of the human body seem unfathomable.

A.M.: I enjoyed the challenge and mystery of science, and biology had a particular draw because it related to the human body and personal experience. As an undergraduate student studying biochemistry, I survived two diagnoses of melanoma. After my close encounter with cancer, I was motivated to more deeply understand this fascinating and sinister disease by focusing my graduate studies in cancer biology. As my thesis 'followed the science', that led to my cell biology work on UNC-45A as a microtubule-destabilizing protein.

A.H.: Since my mother passed away from metastatic breast cancer when I was a little, it was very natural for me to become curious about what killed my mother. When I joined the UNC-45A research project, I was very interested in how UNC-45A contributes to paclitaxel resistance in cancer because my mother used paclitaxel and she developed resistance to it. Therefore, having a close relative who suffered from cancer really motivated me to pursue a career in science.

Who are your role models in science? Why?

A.M.: I greatly appreciated the emphasis on women in science during my education, and the stories of Rosalind Franklin and Marie Curie's major contributions really stuck with me as inspiration. One discovery can change the course of science.

What's next for you?

A.H.: In this study, we have seen UNC-45A-overexpressing cells have more curved microtubules; therefore, the next thing would be to study if more curved microtubules are independent of the effects of non-muscle myosin II. For me personally, I will apply to PhD programs in the US.

J.H.: I am in my final year of medical school. After graduating, I plan to work in the field of neurology or psychiatry and to work as a clinician and do research.

A.M.: I finished my PhD in May of 2019 and pivoted to a career as Director of Grants for Superior Medical Experts, where I assist healthcare startups in applying for SBIR/STTR grant funding for their high-risk innovations. This was motivated by my passion for scientific communication and variety; I love learning about several technologies at once that have the potential to shift healthcare as we know it in the near future.

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

J.H.: I used to do boxing for several years (but I was not really successful and was always afraid of my opponents to be honest).

A.M.: Every year over the Thanksgiving weekend, my family and I bake over 1000 Christmas cookies in a single day to share with our loved ones.

A.H.: I like to go to the museum sometimes and make sketches of artworks.

Reference

Habicht, J., Mooneyham, A., Hoshino, A., Shetty, M., Zhang, X., Emmings, E., Yang, Q., Coombes, C., Gardner, M. K. and Bazzaro, M. (2021). UNC-45A breaks the microtubule lattice independently of its effect on non-muscle myosin II. *J. Cell Sci.* **134**, jcs248815. doi:10.1242/jcs.248815