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FIRST PERSON

First person – Catherine (Cathy) Cheng

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. Cathy Cheng is the first author on 'Tropomyosin 3.5 protects the F-actin networks required for tissue biomechanical properties', published in Journal of Cell Science. Cathy did her postdoctoral studies in the lab of Dr Velia Fowler at the Scripps Research Institute, La Jolla, USA, and, in September 2018, joined Indiana University, Bloomington, USA, as an Assistant Professor, where she will continue to investigate the mechanisms for establishing and maintaining lifelong homeostasis and transparency in the eye lens.

Cathy Cheng

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

The actin filament network is required for normal cell structure, function and mechanical properties. The cytoskeleton, including the actin filament network, of the cell is analogous to the wood frame of a house. Tropomyosin is an important building block in the actin filament network, and we showed that tropomyosin is needed for the biomechanical properties of the eye lens. The lens is a transparent organ in the front of the eye that focuses incoming light to form a clear image. The biomechanical properties of the lens are crucial for its focusing ability. There is little known about the cell and molecular mechanisms that support lens biomechanical function, and the increase in lens stiffness with age results in the need for reading glasses. Our work showed that decreased levels of tropomyosin in the lens result in less mechanically stable actin filaments and a decrease in the lens stiffness and resilience (the ability to return to its normal shape after compression). These results show for the first time that tropomyosin is required for normal lens mechanical properties by protecting specific types of actin filament networks. This knowledge helps us understand how the lens establishes its normal mechanical properties.

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

The eye lens is a 3D organ that cannot be recapitulated with 2D cell culture. Thus, our studies required working with whole-lens tissue. We have developed novel ways to study the lens. To measure the biomechanical properties of the lens, our lab perfected a simple and effective method to determine tissue stiffness and shape by compressing the lens with glass coverslips. Lens cells cannot be dissociated for study in a petri dish. Thus, we developed new methods to isolate and immunostain single lens cells to allow for an understanding of the proteins required for the complex membrane contours of these specialized cells.

"The light bulb moment was our observation that… tropomodulin 1, is dissociated from the cell membrane when there is a decrease in tropomyosin."

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

We were puzzled by the lack of an obvious defect in cell morphology and overall lens shape and size, despite decreased stiffness of tropomyosin-deficient lenses. The light bulb moment was our observation that another actin-filament-binding protein, tropomodulin 1, is dissociated from the cell membrane when there is a decrease in tropomyosin. This led us to the discovery that there is a balance of different type of actin filament networks in the lens that are required for the normal biomechanical properties and that a previously unstudied tropomyosin isoform, Tpm3.5, is needed to protect mechanically stable actin filaments in the lens.

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

Journal of Cell Science is a premier cell biology journal with a broad audience. Our work describes the link between subcellular changes to a cell cytoskeleton and the actual function of a biomechanical tissue. We felt this work would be of interest to cell biologists.

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

Dr Song Li (currently at UCLA) was my undergraduate research mentor at UC Berkeley. I completed an undergraduate research honors

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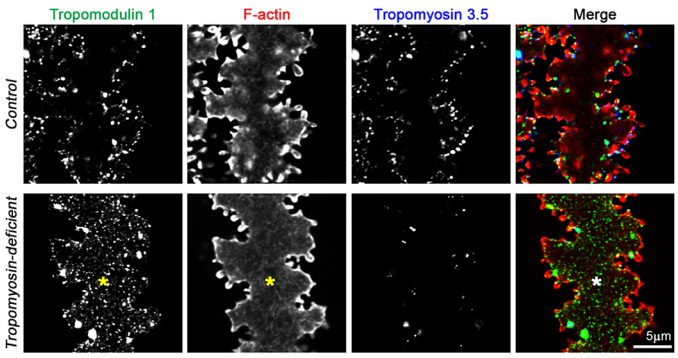

Tropomodulin 1 and tropomyosin 3.5 are actin filament (F-actin)-binding proteins that affect filament length and stability. Tropomodulin 1 (green) is colocalized with tropomyosin (blue) and F-actin (red) at the membrane of control lens fiber cells and dissociates from the membrane in tropomyosin-deficient lens fiber (asterisk).

thesis in his lab studying adult stem cell differentiation induced by mechanical stretch. Owing to the small size of his lab at that time, I was able to run the project by myself with direct supervision from him. He emphasized the experiments were not just a set of protocols, but that one should understand the underlying reasons for each step of a process. That deeper understanding allowed experiments to be tweaked and perfected as we developed the project. I fell in love with research while working in his lab and decided to pursue a graduate degree. He was instrumental in my graduate career, serving on my PhD qualifying exam committee and being a faculty advisor.

“The idea for a new protocol to immunostain lens cells came to me in the shower!”

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?

One of my favorite aspects of research is learning new things every day. It is always an adventure. You never know where your results will take you, and you never know when inspiration will strike. The idea for a new protocol to immunostain lens cells came to me in the shower! Research is not just about the individual, rather it is a team effort. It is a giant jigsaw puzzle of parallel discoveries where all of the piece fit into a bigger picture. It is remarkable to be a small part of the overall puzzle.

Who are your role models in science? Why?

Dr Velia Fowler is not only an outstanding scientist, but also a steadfast leader and mentor whom I deeply admire and emulate. Academic research is a particularly difficult road because it takes not only a love for science and learning, but creativity and perseverance. Velia is always pushing the limits of technology and encourages experimentation. She sees failed experiments as a learning opportunity rather than one of discouragement. She gave me the freedom to utilize my unique skill set to develop novel ways to study the lens and tackle technical problems with new and inventive protocols. Her infectious enthusiasm for science and learning and her courage to try new ideas have served as a driving force and inspiration for everyone who works with her. She is undoubtedly the best role model that I have encountered, and I want to emulate both her scientific ingenuity as well as her knack for steering projects into new and exciting areas.

What’s next for you?

I recently joined the faculty at Indiana University, Bloomington in the School of Optometry as a tenure-track assistant professor. I will be starting a new research lab and focusing on Eph–ephrin bidirectional signaling in eye lens homeostasis and transparency.

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

My hobby is jewelry making, ranging from beading to simple wire work. My friends and family have been the lucky recipients of custom-designed pieces.

Reference

Cheng, C., Roberta, B., Nowak, R. B., Amadeo, M. B., Biswas, S. K., Lo, W.-K. and Fowler, V. M. (2018). Tropomyosin 3.5 protects the F-actin networks required for tissue biomechanical properties. *J. Cell Sci.* **131**, jcs222042.