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FIRST PERSON

First person – Ambuja Navalkar

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. Ambuja Navalkar is first author on 'Oncogenic gain of function due to p53 amyloids occurs through aberrant alteration of cell cycle and proliferation', published in JCS. Ambuja conducted the research described in this article while a postdoctoral fellow in Professor Samir K. Maji's lab at the Indian Institute of Technology Bombay, Mumbai, India. She is now a postdoctoral research associate in the lab of Professor Tanja Mittag at St. Jude Children's Research Hospital, Memphis, TN, USA, investigating the role of biomolecular condensation in transcription factor assembly and activity in the context of cancer.

Ambuja Navalkar

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

Cancer is an intricate disease that has been extensively studied for several decades without any development of a substantial tool for its elimination. Various biological pathways and proteins have been implicated in the unlimited proliferation of cells that leads to tumor formation. One such protein, p53, has been shown to protect cells from forming tumors. p53 is known to become misfolded and lose its structure, thereby affecting its native tumor-suppressive function, in a plethora of cancers. We wanted to understand whether the formation of p53 amyloid aggregates is directly linked to the loss of native p53 function.

We have previously shown that p53 amyloid formation triggers the oncogenic phenotype of cells. These p53 amyloids can act as prions by transferring oncogenic properties to the next generation of cells. Moreover, injecting cells with p53 amyloids in mice also leads to tumor formation.

In our current study, we aimed to decipher the signaling pathways that cause this cellular transformation by amyloids. By mapping changes in mRNA and protein levels, we found the pathways that are dysregulated upon p53 amyloid formation. In a physiological context, our results help explain how cells with p53 amyloids can gain cancer-like properties. We can use our understanding of which pathways are altered to selectively target cancer transformation in cells with p53 amyloids.

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

The journey of this work had its ups and downs, especially since it was carried out in the midst of a pandemic. To study the pathways causing the oncogenic changes in cells, we needed a global screening approach. We addressed this by using microarray and proteomic platforms, which had never been used by our lab before and, hence, were challenging. Multiple collaborations with other institutes and teamwork in our lab helped us to overcome this hurdle. We were able to successfully demonstrate which pathways were altered due to p53 amyloids in the cells by combining the microarray and proteomic data. I am incredibly grateful to our collaborators, who worked tirelessly to achieve this.

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

Journal of Cell Science has always been regarded as a journal with prestige and with high-quality scientific papers that address diverse topics in cell biology. We have previously published in Journal of Cell Science with a streamlined review process and an efficient publication timeline. Hence, we chose Journal of Cell Science because we believe that our work will be showcased to a wide audience in the fields of protein aggregation, cell biology and cancer. Additionally, I appreciate the platform of the First Person interviews given to early-career researchers so they can broadcast their research.

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

I have had a significant journey in Dr Maji's lab during my graduate studies and in my postdoctoral venture. Dr. Maji is self-driven and has helped me to overcome many barriers with his persistence. All the lab members have been extremely supportive both in and out of the lab. I gained a lot from their experience in the field, as well as from their scientific passion and commitment. The training, particularly from other postdocs in the lab, was special because, in addition to research expertise, it taught me how to manage a lab,

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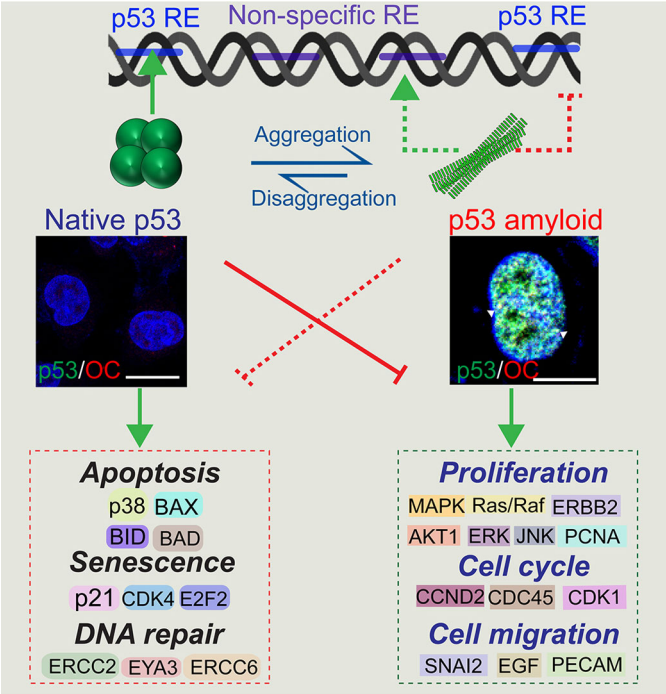

p53 amyloid formation alters the native p53 transcriptional landscape and activates tumorigenic pathways. Left panel shows basal levels of p53 and native p53 functions; right panel shows amyloid-specific (OC-positive) p53 amyloid aggregates (arrowheads), which alter cellular pathways. Scale bars: 10 µm.

how to apply for grants and other skills that will help me in the academic path ahead.

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?

Biology has always fascinated me, especially the evolutionary aspect. I was intrigued by how organisms develop by implementing adaptive strategies. As a child, I was curious about the role of genetics in shaping the survival of organisms. The most pivotal moments were in my early days as a graduate student when I did basic cloning of genes. I was fascinated with the answers I got from these ventures. It is an enthralling experience to think of a question and discover means of finding answers – like completing a big puzzle with several small pieces. I still have the same enthusiasm daily to do experiments, as they answer so many questions about the world we are living in. I hope to nurture this curiosity and way of thinking as well as enjoy science with outstanding peers in my journey ahead.

Who are your role models in science? Why?

I feel motivated by people who feel that science is not their livelihood but a philosophy of their life. I am also inspired by thinkers who have deep insights into the workings of nature and profoundly impact the world with their thoughts – Charles Darwin, Richard Feynman, Stanley Prusiner, Elizabeth Blackburn and Richard Dawkins, to name a few. I am also impressed by Jennifer Doudna's research and contributions to science.

What's next for you?

Currently, I am working with the scientifically driven team of Professor Tanja Mittag as a postdoctoral research associate at the St. Jude Children's Research Hospital in Memphis, USA. I am keen to explore the involvement of biomolecular condensation in transcriptional factor activity in the context of cancer. In the future, I want to stay connected to research and do research that excites me, daily.

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

I enjoy reading mystery novels and solving puzzles. I also like traveling to new places and exploring local cuisines. I hope to travel around the world and build a repertoire of enriching experiences.

Reference

Navalkar, A., Paul, A., Sakunthala, A., Pandey, S., Dey, A. K., Saha, S., Sahoo, S., Jolly, M. K., Maiti, T. K. and Maji, S. K. (2022). Oncogenic gain of function due to p53 amyloids occurs through aberrant alteration of cell cycle and proliferation. *J. Cell Sci.* **135**, jcs259500 doi:10.1242/jcs.259500.