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FIRST PERSON

First person – Akash Chinchole

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. Akash Chinchole is first author on 'MLL regulates the actin cytoskeleton and cell migration by stabilising Rho GTPases via the expression of RhoGDI1', published in JCS. Akash is a PhD student in the lab of Dr Shweta Tyagi at Centre for DNA Fingerprinting and Diagnostics, Hyderabad, India, where he is interested in studying disease models pertaining to defective cell migration and developing therapeutics.

Akash Chinchole

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

Cancer can be lethal, and the surprising ability of cancer cells to move from one tissue to another (metastasize) makes it worse. Just like animals have feet to help them walk, in cells, there are similar structures, such as lamellipodia. Actin fibers and myosin motors act as 'bones and muscles' in lamellipodia. We show that MLL is required to form actin fibers and that it acts by controlling the protein level of certain members of the Rho GTPases family in the cell. Without MLL, the cells cannot acquire a 'normal' shape or walk. Targeting or inactivating MLL with a drug prevents certain cancer cells (like those from breast cancer) from multiplying and forming larger tumors.

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

In my lab, we not only study the conventional transcriptional aspect of the MLL protein but also look at its unconventional roles in maintaining cell homeostasis. My project started based on a mass spectrometric study indicating that the MLL complex interacts with many GEFs (activators of Rho GTPases) that might have a role in mitosis. After many twists and turns, I realized that I might be dealing with Rho GTPases directly. This project came with its own set of challenges. Firstly, I was the only student in the lab working on Rho GTPases, and I had to standardize and perform many related assays on my own. Second, and the more important challenge, was to pinpoint which one out of the 22 known Rho GTPase to investigate! Roughly, all the phenotypes seen upon MLL depletion, pointed towards involvement of RhoA. Thanks to my guide's careful analysis of my results and her insistence on studying other family members as a control, we eventually ended up studying not one but three Rho GTPases and one Rho GDP dissociation inhibitor (Rho GDI).

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

There were not one but two eureka moments for me. As I said earlier, we started off by looking at the role of MLL in the regulation of the Rho GTPase RhoA. But over time, I found that all three of the best characterized Rho GTPases, RhoA, Rac1 and Cdc42, were regulated by MLL. This was the first time we realized that MLL had a more central role in regulation of Rho GTPases. As MLL did not regulate the transcripts of the Rho GTPase but its SET domain was involved, I spent considerable time looking for a reason. Finally, when I found out MLL's involvement in transcriptional regulation of a chaperone (RhoGDI1), it was the last piece of this puzzle!

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

My project involved various aspects of Rho GTPase biology, transcription and xenograft studies. Hence, we were looking for a journal with wide readership. JCS is a reputed journal in the field of cell biology. It's fair, transparent, and a quick peer review process with an academic editor is also a plus.

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

My interactions with my PhD supervisor Shweta Tyagi have shaped my scientific thought process. She has always encouraged me to follow my own scientific path, propose my hypothesis, yet have the courage to move on if it fails. Her insistence on 'quality over quantity' has driven me to perform better. Mentors come in all forms. Even by hanging out with my friends and discussing experiments during a tea break, I have learnt many things! One instance comes to mind when I was discussing my project with a friend, and he suggested that I perform a Boyden's chamber assay

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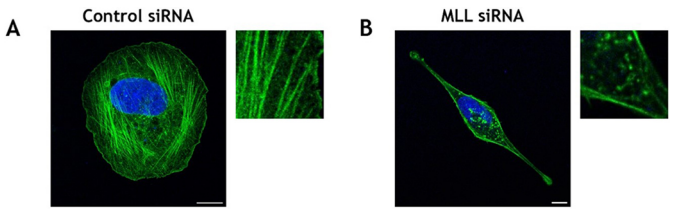

Depletion of MLL causes profound changes in cell shape and actin stress fiber formation.

for cell migration. This experiment later proved to be one of the most important ones in our study.

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?

As a child, I grew up watching my grandfather work in his laboratory. Back in the day, he was a PhD student at National Chemical Laboratory, Pune, and later pursued a career in industry. He would take me to his lab and show me little 'magic tricks' of solutions changing colors after titrations. Science was fun when he taught it. That is what led me on this path. Watching him ponder over a problem that he would face in his lab and seeing the satisfaction on his face when he would eventually solve it gave me immense motivation even during my PhD.

Who are your role models in science? Why?

Apart from my grandfather, I was fascinated by the work of Gregor Mendel. Principles of heredity as we know today, are based on his ingenious experiments completely driven by his curiosity.

What's next for you?

During my PhD, my interests have grown towards cell migration in neurodevelopment and I want to apply the findings in translational medicine. I will be submitting my thesis soon and plan to apply for post-doctoral positions.

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

I love watching the National Geographic channel and going on jungle safaris. I would someday like to work on a wildlife conservation program.

Reference

Chinchole, A., Lone, K. A. and Tyagi, S. (2022). MLL regulates the actin cytoskeleton and cell migration by stabilising Rho GTPases via the expression of RhoGDI1. *J. Cell Sci.* **135**, jcs260042. doi:10.1242/jcs.260042