

FIRST PERSON

First person – Roopali Pradhan

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. Roopali Pradhan is first author on 'Lamin A/C modulates spatial organization and function of the Hsp70 gene locus via nuclear myosin I', published in JCS. Roopali conducted the research described in this article while an integrated MS-PhD student in Dr Kundan Sengupta's lab at Indian Institute of Science Education and Research (IISER), Pashan, Pune, India. She is now a postdoctoral research associate in the lab of Prof. Julie Ahringer at Wellcome Trust/Cancer Research UK Gurdon Institute, UK, where she is interested in understanding chromatin organization across development and ageing, particularly the regulation imparted by nuclear landmarks and transcriptional activity in shaping local and global genome architecture.

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

A 'heat shock' response (HSR) is activated in organisms to counter different types of extraneous stresses. The trigger does not necessarily have to be elevated temperature (contrary to what the name suggests), but also includes an increase in free radicals and heavy metal ions. As a part of this response, specialized heat shock proteins (Hsps) are expressed that protect other cellular proteins and the DNA from detrimental effects of extraneous stress. Production of the Hsps and their import into the nucleus are important steps in the HSR, and are finely regulated in cells. In this study, we examined whether these steps could be modulated by a protein that is vital for maintaining nuclear structure and function, lamin A/C. It has been shown previously that cells derived from Hutchinson–Gilford progeria syndrome patients – caused by mutation in the *LMNA* gene encoding lamin A/C – are hypersensitive to heat shock. We were therefore curious to understand the regulatory crosstalk between lamin A/C and the HSR, and found that lamin A/C acts via a nuclear motor protein, nuclear myosin I, to modulate the spatial positioning of the Hsp70 gene locus following heat shock, which also impacts its expression levels.

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

It was challenging to adapt the downstream biochemical and microscopy-associated assays to the time, temperature and experimental regime that we were following for heat shock induction. This was particularly true for the Immuno-3D fluorescence *in situ* hybridization (FISH) protocol wherein we visualized the nuclear lamina, the SC35 speckles and the Hsp70 gene locus together. We optimized every step during both the immunofluorescence assay and *in situ* hybridization to ensure that the combined protocol gave a good signal for the gene locus, as well as the simultaneous immunostaining.

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Roopali Pradhan

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

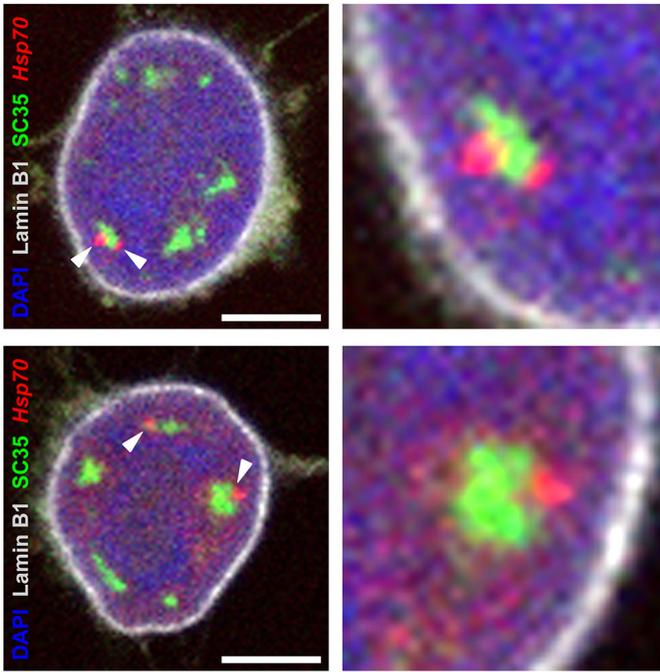
The result that stuck with me was that, although the independent knockdowns of all three lamins (A/C, B1 and B2) led to an attenuation of the *HSPA1A* or *HSPA1L* expression levels upon heat shock, it was only the loss of lamin A/C that abrogated the spatial repositioning of the Hsp70 gene locus. This was the starting point that actually drove us to investigate how lamin A/C could be contributing to the regulation of the expression and dynamics of the Hsp70 gene locus.

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

I have always enjoyed reading articles published in JCS as they generally employ a combination of biochemistry and molecular biology techniques along with high-resolution microscopy. The journal caters to a wide audience in the field of cell biology, as well as offering fast decision times and excellent publication practices. JCS was an easy and early choice.

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

I believe that a supportive lab environment contributes to making scientific research stress-free. I am very lucky to have been a part of a chromosome biology lab during my PhD, where helping each other out was like second nature to everyone in the lab, and my PhD supervisor Dr Kundan Sengupta strongly encouraged this. While everyone in the lab has been kind enough to help me out in some way or the other, I am particularly thankful to my senior colleague Devika for her invaluable scientific and technical guidance in my early years as a PhD student. It made me more competent and insightful in designing experiments and in keeping abreast of the current literature. I would also like to mention Dr Girish Ratnaparkhi,



Immunostaining followed by 3D-FISH. The image depicts the spatial organization of the Hsp70 gene locus with respect to the SC35 nuclear speckles and the nuclear lamina (marked by lamin B1).

who has always been an excellent mentor and advisor with his science and life lessons.

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?

Joining an integrated MS-PhD program was not something that I had planned. But becoming a part of IISER Pune and being exposed to basic science research for the first time made me realize that I loved it. Every experimental result has been an interesting moment on this path, and what has led me on so far has been the curiosity to perform an experiment and seeing what happens.

Who are your role models in science? Why?

I don't have any specific role models, rather I admire and respect anyone who pursues a career in scientific research despite its highs and lows. I do immensely enjoy reading books by Bernd Heinrich and find his work quite fascinating.

What's next for you?

I have recently joined Prof. Julie Ahringer's lab at the Gurdon Institute, University of Cambridge as a postdoctoral researcher.

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

I love reading, playing badminton and watching anime in my free time

Reference

Pradhan, R., Nallappa, M. J. and Sengupta, K. (2020). Lamin A/C modulates spatial organization and function of the Hsp70 gene locus via nuclear myosin I. *J. Cell Sci.* **133**, jcs236265. doi:10.1242/jcs.236265