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FIRST PERSON

First person – Indrasen Magre

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. Indrasen Magre is first author on 'Nup358 regulates microridge length by controlling SUMOylation-dependent activity of aPKC in zebrafish epidermis', published in JCS. Indrasen completed his PhD in the lab of Dr Jomon Joseph at National Centre for Cell Science, Pune, India, where he was involved in dissecting molecular mechanisms governing cell polarity during development.

Indrasen Magre

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

Cell polarity is fundamental to all forms of life. Asymmetric, yet non-random distribution of cellular structures, such as organelles and cytoskeleton, forms the basis for generation and maintenance of cell polarity. Actin-rich microridges present on the apical surface of zebrafish peridermal cells are one example of a polarized cellular structure. Seminal findings from the nematode *Caenorhabditis elegans* and further studies in other model organisms have revealed that a set of key players, generally referred as polarity proteins, are instrumental in regulating cell polarity. Previous studies from Dr Mahendra Sonawane's lab demonstrated that the polarity protein atypical potein kinase C (aPKC) is involved in restricting the length of peridermal microridges in zebrafish by inhibiting another polarity protein, Lgl. Meanwhile, our lab had shown that aPKC is post-translationally modified by a ubiquitin-like protein called SUMO (SUMOylation) and that the E3 ligase Nup358 is involved in this process. In this study, we show that Nup358-mediated SUMOylation of aPKC is important in maintaining the microridge length. These microridges are also seen on other epithelial surfaces, like the mucosal cavity, vaginal epithelium, esophageal lining and many of the non-keratinized squamous epithelium tissues, where they are thought to play a role in mucous retention, membrane storage and abrasion resistance. This study not only sheds light on the intracellular factors regulating microridge structure, but is also an important step towards understanding the molecular basis of microridge-associated diseases, such as esophagitis, dry eye, dry mouth and others.

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

Since this was a collaborative project with Dr Mahendra Sonawane (Tata Institute of Fundamental Research, Mumbai), one or the major challenges for me was to shuttle between two labs and to learn the techniques pertaining to working with zebrafish. Mahendra and all the students in his lab were extremely helpful, and we had a very healthy and interactive collaboration. Another challenging part of the project was the quantitation of microridge lengths. Owing to the large extent of variation in microridge lengths between different clutches of embryos, different embryos of the same clutch and even different cells of the same embryo, we had to take a large number of microridges (5000–10,000) into consideration per test group of each experiment. Help from Vikas and Indraneel was instrumental in speeding up this part of the project. Synthesizing ∼11 kb-long full length GFP–hNup358 mRNA and microinjection into zebrafish embryos were other challenges. It took almost a year to standardize this experiment.

"…I was really thrilled to see the long microridge phenotype in Nup358 morphants. It was the very first experiment of the project…"

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

I was excited by every result that we got as it would add a missing piece to the puzzle. To mention a special instance, I was really thrilled to see the long microridges phenotype in Nup358 morphants. It was the very first experiment of the project; the phenotype was very striking and got me interested in looking at microridges further. Results we obtained using the Lgl mutant not only supported our hypothesis but were also in line with the previous finding from Mahendra's lab. This experiment actually boosted my confidence in the hypothesis and was a defining moment in the project. It was also great to see human Nup358 being able to rescue the long ridge phenotype caused by the depletion of

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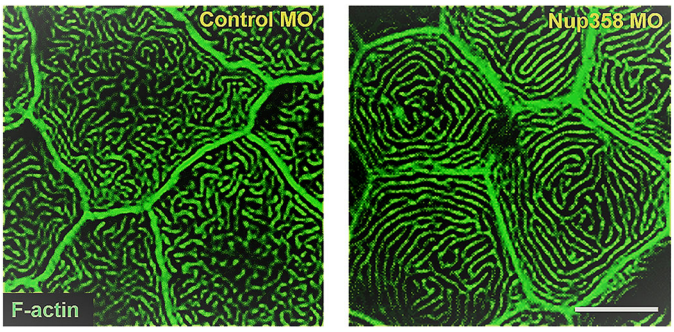

Microridges present on the apical surface of perdermal cells of zebrafish embryos. Embryos were injected with either control (Control MO), or Nup358 (Nup358 MO) morpholino. The microridges (green) were visualized by phalloidin staining.

zebrafish Nup358, highlighting the conservation of function. It was also gratifying to see that the function of Nup358 in microridge regulation was dependent on its SUMO E3 ligase activity.

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

This is one of the best journals that publish scientifically relevant papers in the field of cell biology. A great feature of Journal of Cell Science is that the manuscripts are handled by practising scientists, who I believe can evaluate the worthiness of the findings more appropriately.

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

Help from my PhD mentor Dr Jomon Joseph was instrumental in the conceptualization and completion of this project. He not only supervised the project but also motivated me through all the ups and downs. His passion and dedication for science is infectious. The lab environment really boosted scientific exchange between the members, and I have learnt different aspects of doing science here. The extensive lab seminars that we had on a weekly basis were very helpful in trouble shooting, as well as getting new ideas. I fondly remember our frequent meetings with Mahendra at different stages of the project. His expertise in the field was very valuable in the shaping up of this project. I am grateful to Mahendra and his lab members for accommodating me in their lab and allowing me to work on such a fascinating project. Constructive criticism from Dr Vasudevan Seshadri during Journal club meetings helped me a lot. Convincing him was a big achievement as he would critically check all the controls and come up with alternative explanations for the same results. I would also like to give a special mention about Renuka, Pratik and Clyde from Mahendra's lab, who have taught me all about working with zebrafish and microridges in the initial days. I was also fortunate to learn RNA techniques from Manas in our lab, who I believe has one of the finest hands.

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?

Back in school, we were shown the typical diagram of a cell with all its organelles. I wondered how all these constituents could fit into a cell. During college days, I was introduced to microscopes and the earlier question was partly answered, but how these individual cells in a multicellular organism function in a coordinated manner intrigued me. Another interesting question that puzzled me was how molecular details of protein interactions are uncovered. I wondered, if viewing a cell itself is difficult, how do people understand the details of protein interactions that occur within the cell? Then there was just one solution, to meet the people who work on these aspects, ask them and learn from them, and that's how I got into science. The fact is, I have more questions now than I had earlier.

Who are your role models in science? Why?

I do not have any particular role model, however, I feel that every person I came across during my journey has inspired me in some way or the other. I was fortunate to learn the ABC of research from my mentor, Dr Jomon Joseph. I am inspired by his passion for science, his lab management skills and dedication. He understands that every person is different and guides each one of us to progress on the path we opt for. He ensures that a healthy lab atmosphere prevails, which helps us to develop ourselves personally and professionally and come up with the best we can. I am also inspired by the novel and high quality work from the labs of Antonio Giraldez and Didier Stainier.

What's next for you?

I will be joining Dr Michel Bagnat's lab soon as a postdoctoral fellow.

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

When I am not in the lab, I love spending time with my family and catching up with old friends. I like exploring new places and trekking on weekends. Playing any sport or exercising is a stress buster for me.

Do you have any message for newcomers in the field of research?

Publishing a paper or completing a degree is definitely a great thing to achieve while you do research, but the bigger aim should be to learn the right things and work with responsibility. Enjoy your work, discuss it with people working in the field, share your ideas and contribute to someone else's work, take a small break when things are not working out and celebrate your success with everyone.

Reference

Magre, I., Fandade, V., Damle, I., Banerjee, P., Yadav, S. K., Sonawane, M. and Joseph, J. (2019). Nup358 regulates microridge length by controlling SUMOylation-dependent activity of aPKC in zebrafish epidermis. *J. Cell. Sci.* **132**, jcs224501. doi:10.1242/jcs.224501