

FIRST PERSON

First person – Shivnarayan Dhuppar

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. Shivnarayan Dhuppar is first author on 'Investigating cell cycle-dependent gene expression in the context of nuclear architecture at a single-allele resolution', published in JCS. Shivnarayan is a postdoc in the lab of Dr Aprotim Mazumder at Tata Institute of Fundamental Research, Hyderabad, India, where he likes to think 'how does it work?', with the 'it' being anything from the biology of a cell to its functions and the physics behind them.

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

DNA, the basic unit of heredity, lies behind all the functions (or malfunctions) inside a human cell. But on its own, DNA can do nothing. For its functional roles, DNA has to be transcribed into mRNAs, which in turn are translated into proteins, which are the workhorse of a cell. This combined process, whereby a stretch of DNA called gene is decoded into a protein, is called gene expression. Gene expression is regulated at many levels, most of which can be linked to the position of the gene inside the cell nucleus – where DNA is safely stored in eukaryotic cell – and its temporal position inside its cell division cycle. Cell division is about the process whereby a single cell divides to give rise to two daughter cells (although there are instances where a cell can give rise to more than two daughters). This process of cellular reproduction is called the cell division cycle or, in general, the cell cycle.

In this report, we have standardized a way to study the regulation of gene expression in the context of nuclear architecture (that is, the relative positioning of a gene inside the cell nucleus) and the cell cycle by combining DNA FISH with smFISH and immunofluorescence, together with microscopy-based cell cycle staging, at single-cell resolution. FISH stands for fluorescence *in situ* hybridization. FISH is used to visualize the gene or RNA of choice inside a cell, whereas immunofluorescence is a way to do the same for protein. The technique presented here is an easy way to study not just the mean trends within a population of cells but also the cell-to-cell variability. After all, does the average age of 29 in India mean all Indians are 29?

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

It was indeed difficult to combine 3D DNA FISH with smFISH and immunofluorescence due to the fact that some of the steps involved in a traditional 3D DNA FISH can adversely affect subsequent smFISH and immunofluorescence steps and vice versa. But after 18 months of tweaking the different parameters involved (which were many), I could establish a simple but robust protocol for the same, which can easily be adapted for many other applications.

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Shivnarayan Dhuppar

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

Research, by its very nature, is more about failures than successes. What I mean is that by the time one finds a peak, another gorge stares one in the face, followed by another peak, followed by another gorge and so on and so forth. There is hardly any time to celebrate the successes or mourn the failures. But surely, it is the successes that keep one going and, in that sense, every small victory in the lab has been a eureka moment for that moment. Did they stick with me? For a while, sure! As for THE EUREKA moment, I am still waiting for it.

“As for THE EUREKA moment, I am still waiting for it.”

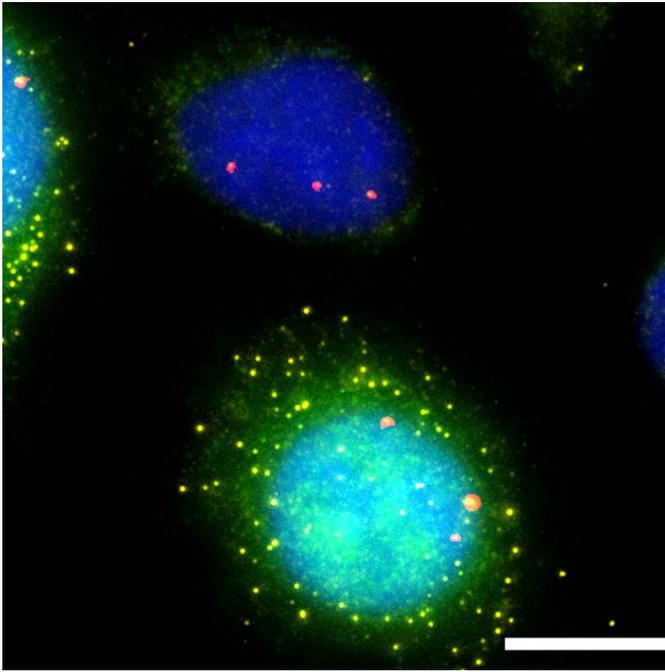
Why did you choose Journal of Cell Science for your paper?

For its quick editorial process and author-friendly policies. JCS has been one of my favorite journals.

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

Dr Aprotim Mazumder, my PhD advisor, has been really supportive throughout my PhD. But beyond the conventional mandate of mentor-mentee relationship, he was open to new ideas and suggestions from me to the extent that he gave me the freedom to design and pursue my own independent projects in the lab. This helped me immensely to grow as an independent and confident scientist.

Dr Sitara Roy also helped me realize the importance of slowing down when the only thing I knew and appreciated was the 'Red Queen



Combined DNA FISH (red), single molecule RNA FISH (yellow) and immunofluorescence (green) for the *CCNA2* gene in hypertriploid HeLa cells. Cell cycle information was obtained by labeling cells with DAPI (blue). Scale bar: 10 μ m.

effect'. Her guidance in and beyond the immediate confines of the lab has always helped me keep the mental strength necessary to continue in this ever changing and highly competitive field of science and research.

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?

My dad, Tilkesh Dhuppar and middle sister, Pooja, were my first science idols, who introduced me to the wonders of

science, especially that of physics and mathematics. They gave me the scientific outlook, curiosity and the thirst to learn and discover new things while my mom, Krishna Dhuppar, and elder sister, Khushboo, gave me the confidence to pursue my dreams. The interesting moment that led me to where I am was my failure at IIT-JEE [entrance examination] after my high school.

Who are your role models in science? Why?

Those who come to my mind at once (not in any particular order) are: Galileo, Newton, Darwin, Maxwell, Riemann, Alan Turing, Einstein, Schrödinger, Homi Bhabha, John Nash, Grigori Perelman, Feynman, N. D. Mermin, Ed Witten, Leonard Susskind, Robert Sapolsky. Surely, I am missing many and the list will swell further as my ignorance shrinks.

If I *have* to call out one name then it will be Prof. Sapolsky for, I believe, it is not just enough to *do* science, one also has to be able to convey its excitement to others while at the same time using it for the benefit of society at large, be it in the form of popular science articles, lectures or public policies.

What's next for you?

I graduated just recently (April 2020), and am currently looking for independent research positions even when I know that the present situation of pandemic is sure to affect, mostly adversely, this search of mine.

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

I want to know everything that is there to know but the sad part is that I have not even started to scratch the surface. In the same vein, I am envious of Stephen Fry's vast knowledge and this keeps me going.

Reference

Dhuppar, S. and Mazumder, A. (2020). Investigating cell cycle-dependent gene expression in the context of nuclear architecture at a single-allele resolution. *J. Cell. Sci.* **133**, jcs246330. doi:10.1242/jcs.246330