

## FIRST PERSON

# First person – Bharath Srinivasan

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. Bharath Srinivasan is co-first author on 'Enrichment of  $Z_{\alpha}$  domains at cytoplasmic stress granules is due to their innate ability to bind to nucleic acids', published in JCS. Bharath conducted the research described in this article while a Marie Skłodowska-Curie Individual Fellow in Alekos Athanasiadis's lab at the Instituto Gulbenkian de Ciência, Oeiras, Portugal. He is now a senior research scientist at AstraZeneca in Cambridge, UK, investigating mechanistic biology and enzymology.

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

When cells face stressful situations, such as viral infection, they create liquid–liquid condensates (something similar to oil droplets in water) that capture RNA and protein molecules to prevent cellular energy being wasted. These structures are called stress granules. The RNA in these stress granules mostly adopts a zig-zag conformation. In this paper, using *in vitro* tools, cell biology and proteomics, we have shown that specific proteins recognize this zig-zag conformation of RNA and localize to the stress granules. This process could be a possible immunological mechanism to prevent viral infection.

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

The most pressing challenge was the untimely demise of the principal investigator on this project. I tried my best in putting together the draft of this paper with the help of my co-first authors and collaborators, and in acquiring the consent of the various stakeholders to get this work published.

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

Usually in scientific pursuits, there is no all-or-nothing result, and sometimes things can get interpretation heavy. When I created a quadruple mutant of a nucleic acid-binding protein and assessed its ability to bind to nucleic acids, I was apprehensive that there would be some residual nucleic acid binding by the mutant that might require explanation. However, the neat all-or-nothing result (whereby the wild-type protein showed binding to nucleic acids and the mutant did not) was very satisfactory!

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

This research pertains to the role of  $Z_{\alpha}$  domains in a cellular process – stress granule biogenesis. The work employed conventional tools of cell biology and proteomics; hence, we believed that Journal of Cell Science would be its most appropriate



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home given the preeminent status of the journal in disseminating cell science research.

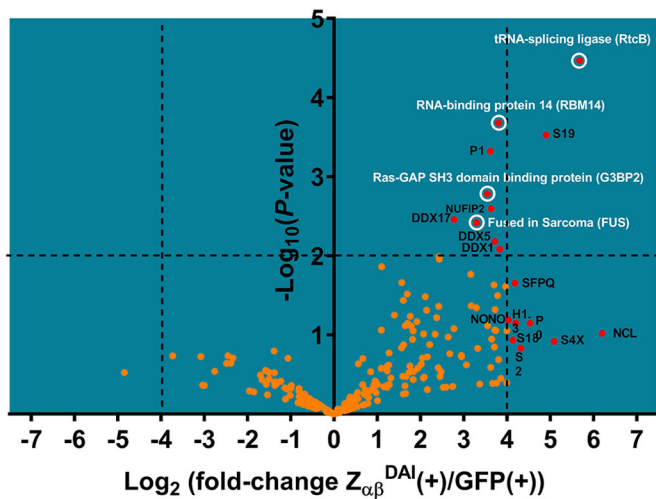
### Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

Dr Lars Jansen and Dr Maria João Amorim were very kind and went out of their way to make time to help by making suggestions and proofreading the manuscript in the absence of Alekos Athanasiadis. I owe an immense debt of gratitude to both of them. The administration at the Instituto Gulbenkian de Ciência (led by the current director Mónica Bettencourt-Dias, deputy director for Science Élio Sucena and former director Jonathan Howard) were also extremely supportive of the whole endeavour. Their guidance and encouragement was special given the atypical circumstances that dictated the communication of this manuscript in the absence of the principal investigator.

### 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?

A career in science entails inquiry, and the desire to know is an ingrained trait of humans. I am no exception to that rule. The moment I realized that a protein molecule was pulsating with life, as evident in the colorimetric signal on a UV/Vis spectrophotometer, I was hooked on science. The second motivational spark was when I first learned to visualize proteins on my computer screen. As part of the work published in our article, I was also exposed to the dazzling multicoloured subcellular world. These moments provided the impetus that still makes me feel excited about the science I pursue.

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Volcano plot of proteomics data showing that  $Z_{\alpha}$  domains interact with prominent markers of stress granules.

### Who are your role models in science? Why?

As a budding biochemist at the Molecular Biophysics unit of the Indian Institute of Science, I was immensely influenced by the herculean effort of G. N. Ramachandran in solving the structure of the collagen triple helix. Further, in response to being challenged by investigators such as Francis Crick and Alexander Rich about the correctness of his collagen structure, Ramachandran developed the Ramachandran plot exclusively based on the principles of 3D geometry. This plot, conceived when hardly any protein structures were available, went on to become the standard for the validation of X-ray crystallographic structures.

J. D. Bernal was another prominent role model in shaping my perception of science. Training with W. H. Bragg, he not only saw

the evolution of X-ray crystallography as a science, but also contributed actively to its growth. His example taught me that effective science does not stop at the laboratory; communicating science to a lay audience, piecing together scientific history and training the next generation are integral parts of being an influential scientist. He trained the likes of Dorothy Hodgkin and published such classics as ‘The Social Function of Science’ and ‘The World, the Flesh and the Devil’.

### What’s next for you?

I have left academia and I am currently working in the pharmaceutical industry at AstraZeneca. The reason I made this transition was to ensure that I concentrate and contribute effectively to the domain of my expertise (mechanistic enzymology), and to see the possible translation of my efforts into a tangible patient therapy in the immediate future.

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

I am passionate about science outreach and teaching, painting, drawing, sculpting, art history and writing literature. An example of my drawing has been highlighted on the cover of The FEBS Journal (volume 288, issue 7; doi:10.1111/febs.15388), and an example of my efforts in science outreach and teaching – ‘Words of advice: teaching enzyme kinetics’ – has recently been published (Srinivasan, 2021). I have also authored and published a work of fiction entitled ‘Formless Meanderings’.

### References

- Gabriel, L., Srinivasan, B., Kuś, K., Mata, J. F., João Amorim, M., Jansen, L. E. T. and Athanasiadis, A. (2021). Enrichment of  $Z_{\alpha}$  domains at cytoplasmic stress granules is due to their innate ability to bind to nucleic acids. *J. Cell Sci.* **134**, jcs258446. doi:10.1242/jcs.258446
- Srinivasan, B. (2021). Words of advice: teaching enzyme kinetics. *FEBS J.* **288**, 2068-2083. doi:10.1111/febs.15537