

## FIRST PERSON

# First person – Arijita Ghosh

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. Arijita Ghosh is the first author on “Leucine-rich repeat-containing 8B protein is associated with the endoplasmic reticulum  $\text{Ca}^{2+}$  leak in HEK293 cells”, published in Journal of Cell Science. Arijita is a PhD student in the laboratory of Amal Kanti Bera at the Indian Institute of Technology Madras, Chennai, India, investigating the role of leucine-rich repeat-containing 8 proteins in cellular calcium homeostasis.

### How would you explain the main findings of your paper to non-scientific family and friends?

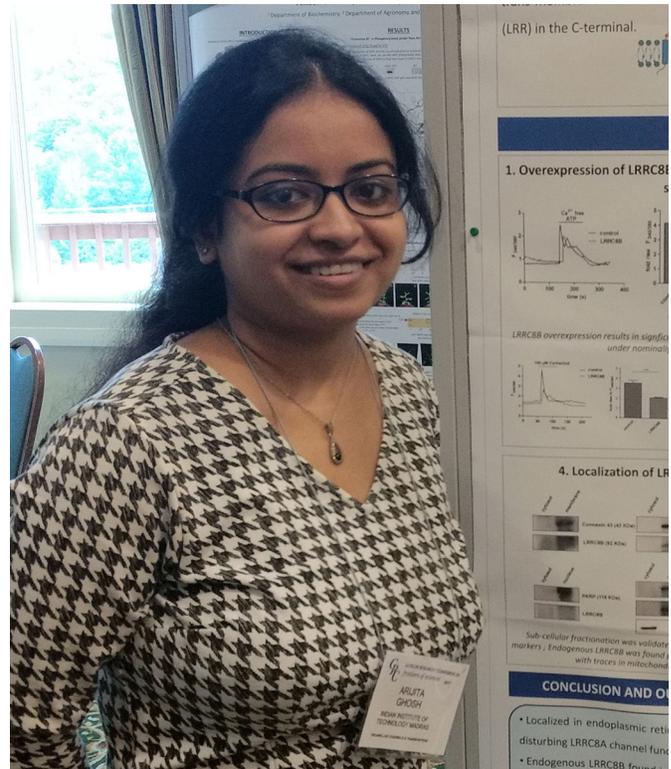
Cells in our body can be compared to our houses. In the same way that houses are surrounded by walls, our cells are protected by a membrane. Houses have doors and windows to let all that we want inside and to keep the unwanted at bay; cellular membranes, too, are equipped with ion channels that regulate the flux of ions between the cell and the exterior. Also, like a house has rooms inside, cells have subcellular compartments that have their own membranes, studded with specific ion channels. One such important subcellular organelle is the endoplasmic reticulum (ER), which serves as a reservoir of  $\text{Ca}^{2+}$  ions and plays an essential role in maintaining the fine balance of  $\text{Ca}^{2+}$  concentration that enables the cell to function properly. We have found that the protein LRRC8B acts as a  $\text{Ca}^{2+}$  leak channel in the ER, thereby causing perturbations in  $\text{Ca}^{2+}$  flux across the cell that further impacts upon other cellular functions.

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

When we started working on this project, there was very little information available on the LRRC8 class of proteins. It was both challenging and exciting to chase the data, but standardisation and experimental aspects took a considerable amount of time and effort. Also, in the initial years of my PhD, I was not confident that these proteins were worth chasing. However, 2014 saw a breakthrough as two very distinguished groups published a major discovery in two top scientific journals where they showed that LRRC8 proteins form a volume-regulated anion channel. This served as a great boost to my motivation and belief in the project and we could continue with increased enthusiasm and anticipation.

Based on pilot experiments, we were able to join the dots and formulate the hypothesis that our protein of interest could be involved in  $\text{Ca}^{2+}$  leak from the ER. The next challenge was to delve into ER  $\text{Ca}^{2+}$  dynamics; ER  $\text{Ca}^{2+}$  leak is an important and enigmatic process about which very little is known. Standardising ER  $\text{Ca}^{2+}$  imaging took us some time owing to certain instrument limitations. Luckily Dr Iino Masumitsu’s discovery of ER-targeted  $\text{Ca}^{2+}$ -sensitive fluorescent protein (CEPIA) constructs in 2014 enabled us to record  $\text{Ca}^{2+}$  changes in the ER more effectively.

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Arijita Ghosh

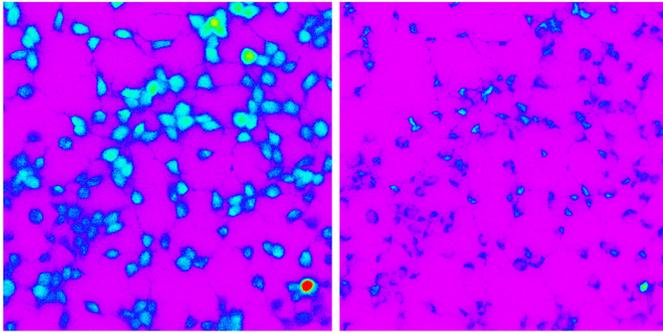
### When doing the research, did you have a particular result or ‘eureka’ moment that has stuck with you?

To find out whether LRRC8B is involved in ER  $\text{Ca}^{2+}$  leak, I was investigating the leak rate after  $\text{Ca}^{2+}$  imaging in the ER. I repeated the experiment in three ways, first with an ER-specific dye (MaggFura) and then with two different ER-targeted  $\text{Ca}^{2+}$ -sensing constructs, RCepiaER and GCepiaER. After analysing the results of the three different data sets I saw a similar significant trend, and that moment was a defining one. I remember bursting into my advisor’s office brimming with excitement to give him the good news!

**“The impossibility of anticipating what you will end up discovering is the most thrilling part of basic research.”**

### Have you had any significant mentors, and how have they helped you?

I have been immensely lucky to pursue a PhD under Dr Amal Kanti Bera, who has been a friend, philosopher and guide in the truest sense of the terms. He has encouraged me during the highs, but most importantly, he has supported me more during the lows. He gave me full academic freedom, which has strengthened my growth as a researcher immensely.



Ca<sup>2+</sup> imaging in ER of HEK293 cells stained with Mag-Fura-2-AM before (left) and after (right) digitonin treatment.

One of my senior colleagues from the lab, Dr Divya Sachidanandan, has played an important role in my research career, from discussing experiments to sharing paper-writing tips. Another significant mentor is Dr Mausita Karmakar, who has helped me with her wise advice right from my college days. I have received help from her on protocols, experiments, choosing labs and every kind of scientific advice possible.

#### **What's the most important piece of advice you would give first-year PhD students?**

A rigorous literature review is one of the keys to fruitful research. It is important to embrace failures and also to celebrate the little joys of PhD life. It is essential to take negatives in your stride and learn from them in order to grow as a researcher. Having faith in

one's project is crucial – if you have strong intuition coupled with sound literature, hard work and preliminary evidence, hold your ground and dig deeper. The impossibility of anticipating what you will end up discovering is the most thrilling part of basic research.

#### **What changes do you think could improve the professional lives of early-career scientists?**

A generous amount of grant funding would help early-career scientists to establish their lab. It is also important they have the money to pursue their own research interests without stringent limitations on project proposals.

#### **What's next for you?**

Currently, I am wrapping up my thesis and will be done with it by the middle of next year. I have started looking for postdoctoral positions and would love to shift to neuroscience and gain experience in optogenetics.

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

I am a trained Indian classical dancer and when I am not engrossed in bench work, I enjoy unwinding to the classical beats of Odissi. Also, I enjoy reading fiction more than scientific papers and I could happily spend my life in a library.

#### **Reference**

Ghosh, A., Khandelwal, N., Kumar, A. and Bera, A. K. (2017). Leucine-rich repeat-containing 8B protein is associated with the endoplasmic reticulum Ca<sup>2+</sup> leak in HEK293 cells. *J. Cell Sci.* **130**, 3818-3828.