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First person – Huildore Bommanna Ranjitha

First Person is a series of interviews with the first authors of a selection of papers published in Journal Cell Science, helping early-career researchers promote themselves alongside their papers. Huildore Bommanna Ranjitha is first author on 'Foot-and-mouth disease virus induces PERK-mediated autophagy to suppress the antiviral interferon response', published in JCS, and is a PhD Scholar in the lab of Dr Suresh H. Basagoudanavar at ICAR-Indian Veterinarian Research Institute, Bengalur, Karnataka, India, performing *in vitro* and *in vivo* analysis of the pathogenesis of animal diseases and working on the development of preventive/diagnostic medicine.

Huildore Bommanna Ranjitha

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

Foot-and-mouth disease is a highly contagious viral disease of cloven footed animals. The disease is caused by foot-and-mouth disease virus (FMDV). We have studied the role of endoplasmic reticulum (ER) stress, the unfolded protein response (UPR) and autophagy during FMDV infection *in vitro*. Disturbance in any of the normal functions of ER causes ER stress and results in an increase in the load of unfolded proteins in its lumen. Furthermore, ER stress activates a cellular stress response known as UPR to reduce the workload and maintain cell viability. The UPR is initiated by the activation of any one of the three UPR stress sensors or, indeed, all of them: inositol-requiring protein 1 (IRE1), protein kinase RNA-like ER kinase (PERK) and activating transcription factor 6 (ATF6). These sensors restore the normal function of ER by halting processes, such as translation, ER-associated degradation (ERAD), an increase in production of chaperones, initiation of autophagy, etc. We found that FMDV induces ER stress and consequently UPR as it utilizes the ER for its multiplication. This in turn activates autophagy via the PERK pathway. The virus-induced PERK-mediated autophagy then reduces the host interferon response, thus promoting virus replication.

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

Treatment with Bafilomycin A1 (100 nM) significantly reduced FMDV infection in cell culture, and this was one of the 'eureka' moments. Subsequently, identification of enlarged ER due to the stress induced during FMDV multiplication in the cells and observation of double membranous autophagy vesicles by transmission electron microscopy confirmed our hypothesis. This was the moment of awe that stuck with me.

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

Journal of Cell Science is an international peer-reviewed scientific journal that covers primary research work related to cellular biology. Our work focused on the novel finding of induction of ER stress and autophagy during FMDV infection in cell culture. Thus we found our work is suitable to publish in the Journal of Cell Science. Also I attended an international conference where one of the invited speakers was Dr Sharon Ahmad, Executive Editor of Journal of Cell Science. She delivered a speech on publishing research work in an academic journal and gave tips on how to prepare a paper and navigate the submission and peer review process, which helped us to design our manuscript so it would be suitable for publication in the journal.

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

We had regular interactions and discussions about the study design and progress of the work with Dr Ravi Manjithaya (one of the authors), whose expertise in autophagy-related pathways and post-transcriptional gene regulation boosted our confidence to continue our research, as autophagy was a new area for our lab. Also, I attended an international conference with scientists from across the country and beyond who added their valuable input, which helped us to improvise our work plan.

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?

Science is all about thrill of inventions and discoveries. It aids in the development of innovative new products and their practical

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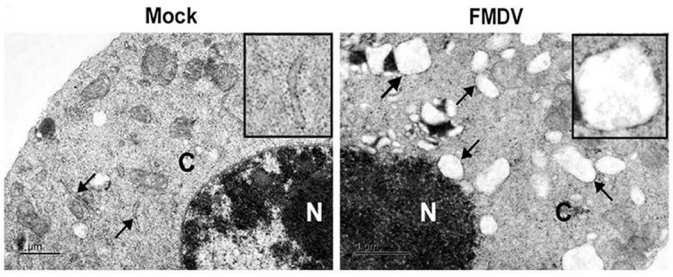

FMDV infection causes ER stress. TEM image showing the normal rough ER (rER; left panel) and dilated rough ER in the FMDV-infected (1 multiplicity of infection, 4 h post infection) cells (right panel). Location of ER indicated by arrow sign. Scale bars: 1 µm. The insets show magnified view of the normal rER (left panel) and dilated rER (right panel). N, nucleus; C, cytoplasm.

use for animals and mankind. These interests made me pursue a career in science. My love of animals and the cloning of Dolly the sheep inspired me to choose research in animal biotechnology.

Who are your role models in science? Why?

I would consider any person who is curious, persistent, dedicated, positive and confident as a role model. In particular my role models are Albert Einstein with his dedication and passion for science, Edison who did not give up and kept doing the work until he succeeded, Abdul Kalam for his inspiring thoughts, Stephen Hawking who defied the odds and continued his research, and many more.

What's next for you?

We are now interested to know the exact mechanism/pathway involved in the modulation of innate immunity by FMDV-induced autophagy. Also, we have planned to carry out the development of an FMDV infectious clone and want to generate deletions to know which region of the virus is involved in the induction of autophagy and to explore the prospects of PERK-mediated autophagy as a target to develop anti-FMDV therapeutics. Further *in vivo* studies are being planned to understand the interplay between RNA viruses and autophagy. Professionally, in the future I am interested in R&D activities related to development of preventive animal healthcare.

Reference

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