

FIRST PERSON

First person – Shalini Roy

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. Shalini Roy is first author on 'Crosstalk of PD-1 signaling with the SIRT1/FOXO-1 axis during the progression of visceral leishmaniasis', published in JCS. Shalini is a PhD student in the lab of Dr Pijush K. Das at CSIR-Indian Institute Of Chemical Biology, Kolkata, India, investigating macrophage biology with an emphasis on understanding disease biology, particularly leishmaniasis.

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

Visceral leishmaniasis is caused by *Leishmania donovani*, an intra-macrophage parasite, and this parasitic disease is fatal when left untreated. A better mechanistic understanding of the disease's progression and propagation will aid us in the identification of drug targets for better therapeutic measures. Evasion of host cell apoptotic death is a key survival strategy adopted by parasites to protect their niche. The precise mechanism of why hosts cells do not undergo apoptosis during the late phase of infection was not known. Our findings revealed, for the first time, that *Leishmania* exploits upregulation of death receptor PD-1 during the later hours of infection to foster a parasite-conducive anti-inflammatory environment. However, despite the activation of the PD-1 pathway, parasites are still capable of preventing cell death because they concurrently upregulate SIRT1, a longevity-inducing factor, during the later hours of infection. This activation of PD-1 and concomitant SIRT1 induction, along with their interplay, helps in disease progression, the detailed mechanism of which is revealed in this work, thus proving PD-1 and SIRT1 could be two important drug targets. The mode of crosstalk between PD-1 and SIRT1 in macrophages is also outlined in the study.

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

The most challenging part of this project was to identify how, despite induction of death receptor PD-1, the infected macrophages did not undergo apoptosis. We overcame this when we identified that SIRT1 induction occurs concomitantly with PD-1 pathway upregulation, during the late hours of infection, which in turn helps to prevent apoptosis of infected macrophages.

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

The particular finding that *Leishmania*-induced SIRT1 induction deacetylates nuclear FOXO-1, which was sequestered into the nucleus owing to activation of PD-1 pathway, and that this



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SIRT1-mediated FOXO-1 deacetylation subsequently also led to inhibition of apoptosis and enhanced disease progression; this result is the 'eureka' moment for us.

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

Journal of Cell Science was chosen because of its prestigious reputation, and also because we wanted our work to reach a broad audience.

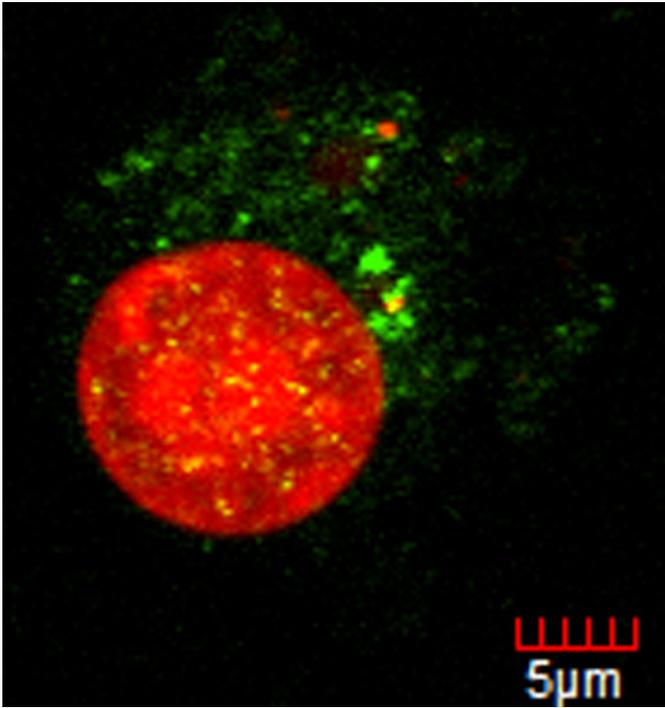
Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

I heartily acknowledge my PhD supervisor, who is the corresponding author of this manuscript, and whose guidance and supervision led to the successful execution and completion of the work. I am also thankful to Dr Anindita Ukil, my co-author, for her critical suggestion and guidance.

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?

I have been eager to pursue a career in science since my early days of post-graduate study, and I am still chasing my dream of being a scientist.

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Leishmania donovani infection-induced SIRT1 did not perturb the nuclear sequestration of FOXO-1.

Reference

Roy, S., Saha, S., Gupta, P., Ukil, A. and Das, P. K. (2019). Crosstalk of PD-1 signaling with the SIRT1/FOXO-1 axis during the progression of visceral leishmaniasis. *J. Cell Sci.* **132**, jcs226274. doi:10.1242/jcs.226274