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FIRST PERSON

First person – Aarthi Subramani

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping researchers promote themselves alongside their papers. Aarthi Subramani is first author on 'Regulation of macrophage IFNγ-stimulated gene expression by the transcriptional coregulator CITED1', published in JCS. Aarthi is a PhD student, graduating December 2022, in the lab of David E. Nelson at the Middle Tennessee State University, Murfreesboro, USA, investigating the interaction of host and pathogen at the cellular and molecular levels, which has always piqued her interest. To be more specific, she is interested in the mechanisms/strategies utilized by either the pathogen or the host during infection and how they shape the outcome of an infection.

Aarthi Subramani

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

The immune cells that protect us from disease-causing pathogens are incredibly diverse, with each type having its own specialized roles. Amongst these, macrophages are especially interesting in that they can dramatically change their roles after exposure to different cytokine signals produced by other immune cells. For example, when they are exposed to IFNγ, they become much better able at ingesting and destroying bacterial and yeast pathogens. Although this activity is important for keeping us healthy, it must be carefully controlled. It has to be vigorous enough to kill harmful microbes, and yet spatially and temporally restricted so that unnecessary inflammation and tissue damage are avoided. One level of control is provided through the expression of CBP/p300-interacting transactivator with glutamic acid/aspartic acid-rich carboxy-terminal domain 2 (CITED2), a protein that limits the expression of proinflammatory genes after macrophages are exposed to IFNγ. In this study, we found another member of CITED family of proteins does the opposite of CITED2. We show that macrophages exposed to IFNγ for extended periods of time (>24 h) express CITED1, and this increases the expression of a subset of proinflammatory genes. In this way, we believe that the balance of CITED1 and CITED2 expression helps to shape the phenotype of macrophages in response to signals produced by our immune cells.

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

RAW 264.7 cells, the macrophage model used in this study, are particularly difficult to transfect, making it challenging to introduce expression plasmids into these cells or even perform gene editing. To overcome this issue, we switched to lentiviral transduction at the start of the project and used dox-inducible constructs to modify the levels of CITED1 in our system.

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

Initially, we thought *C. neoformans* infection was the only inducer of CITED1 expression, but further studies revealed that IFNγ alone could also stimulate CITED1 in macrophages. This was interesting, as it suggests the importance of CITED1 proteins in regulating the macrophage proinflammatory function. Another moment came while measuring the effect of ectopic CITED1 expression on IFNγ-stimulated gene expression. CITED2 limits proinflammatory gene expression by repressing the activities of the NF-κB, STATs and IRFs in myeloid cells. Because of the structural similarities between the two CITED proteins, we expected CITED1 to behave in a similar way. To our surprise, CITED1 heightened the expression of genes associated with the IFNγ response, STAT1 and IRF1-regulated gene sets. It is exciting as CITED1 was not thought to be expressed in macrophages prior to this project.

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

We decided to publish our findings in the Journal of Cell Science as it covers a broad spectrum of themes pertaining to cell biology, is dedicated to admitting high-quality scientific research and caters to a wide variety of readers.

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

When I joined the lab of Dr Nelson as a PhD student, I received a lot of support from lab members and other collaborators of this project. My advisor, Dr Nelson, has been a source of motivation for me and has inspired me to be the very best version of myself that I am capable of being at all times. Dr McClelland and

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Dr Seipelt, who are collaborators on the project, have been of tremendous assistance to me and have steered me in the right direction.

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?

While participating in a science fair organized at my school, a particular display caught my eye – colorful swirls with crisscrossing lines and bright recurring letters '**A T G C**' splashed on the side. This was my first love of science. Slowly, the interest grew and moved towards infections and immunity. The interaction of immune cells in response to pathogenic illnesses has always captivated me. This interest has led me to pursue a PhD, and fortunately, I joined a lab that was doing a similar line of research.

What's next for you?

I am moving to Duke University for a postdoc position and am excited about this opportunity.

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

I am a trained dancer and have a great passion for dance. More recently, I've developed a liking for traveling. I've always enjoyed getting dressed up and posing for photos since I was little. Travel and pictures: I couldn't ask for a better combo!

Reference

Subramani, A., Hite, M. E. L., Garcia, S., Maxwell, J., Kondee, H., Millican, G. E., McClelland, E. E., Seipelt-Thiemann, R. L. and Nelson, D. E. (2023). Regulation of macrophage IFNγ-stimulated gene expression by the transcriptional coregulator CITED1. *J. Cell Sci.* 136, jcs.260529. doi:10.1242/jcs.260529