© 2022. Published by The Company of Biologists Ltd | Journal of Cell Science (2022) 135, jcs260115. doi:10.1242/jcs.260115

FIRST PERSON

First person – Raviprasad Kuthethur

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. Raviprasad Kuthethur is first author on 'Expression analysis and function of mitochondrial genome-encoded microRNAs', published in JCS. Raviprasad is a PhD scholar in the lab of Dr Sanjiban Chakrabarty at Manipal School of Life Sciences, Manipal Academy of Higher Education, Karnataka, India, investigating the function of mitochondrial genome-encoded microRNAs in mitochondrial perturbation.

Raviprasad Kuthethur

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

Mitochondria are the cell's powerhouse, responsible for producing energy in all eukaryotic cells. Owing to their small-sized genome, many of the functional requirement of mitochondria are governed by the nuclear genome. This nuclear-to-mitochondria crosstalk is known as anterograde signaling. Some of these signaling processes are regulated by microRNAs (miRNAs). Most of the miRNAs identified inside mitochondria come from the nucleus. We have identified 13 mitochondrial-genome-encoded miRNAs (mitomiRs) that are differentially expressed in breast cancer cells. Interestingly, mitomiRs are associated with the RNA-induced silencing complex (RISC) and travel to the cytoplasm. We have also shown that mitomiRs regulate mitochondrial DNA copy number by regulating PPARGC1a expression and function in breast cancer cells. We believe that mitomiRs might play a significant role in regulating mitochondria in various pathophysiological conditions.

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

Assessing the relative abundance of novel mitochondrial-genome-encoded miRNAs (mitomiRs) in different breast tumor subtype-specific cell lines and tissue specimens was quite a straightforward experiment. However, analyzing the association of mitomiRs with Ago2, a RISC component, inside mitochondria was relatively challenging as the composition and abundance of RISC components inside mitochondria are relatively unknown. We showed that mitochondrial Ago2 physically interacts with mitomiRs. Subsequently, a cell line expressing mitochondria-targeted Ago2 was generated to confirm mitomiR association with Ago2 inside mitochondria. These experiments provided conclusive evidence of Ago2–mitomiR association both in the cytoplasm and the mitochondria.

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

The idea that mitochondria can make their miRNAs and that their abundance is critical for mitochondria function was a relatively new concept when we started this project. There were several moments throughout the project that motivated me to proceed further. One such moment was when I visualized mitomiR-5-5p localization inside mitochondria using confocal microscopy. After struggling for more than a year, I was elated when I generated a stable mitomiR-5-5p sponge model. I could feel the butterflies in my stomach when I was about to observe the results of the experiment after all the struggles.

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

Journal of Cell Science is one of the most impactful journals in the cell biology field. It publishes excellent research articles and covers a wide range of topics for a diverse audience.

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

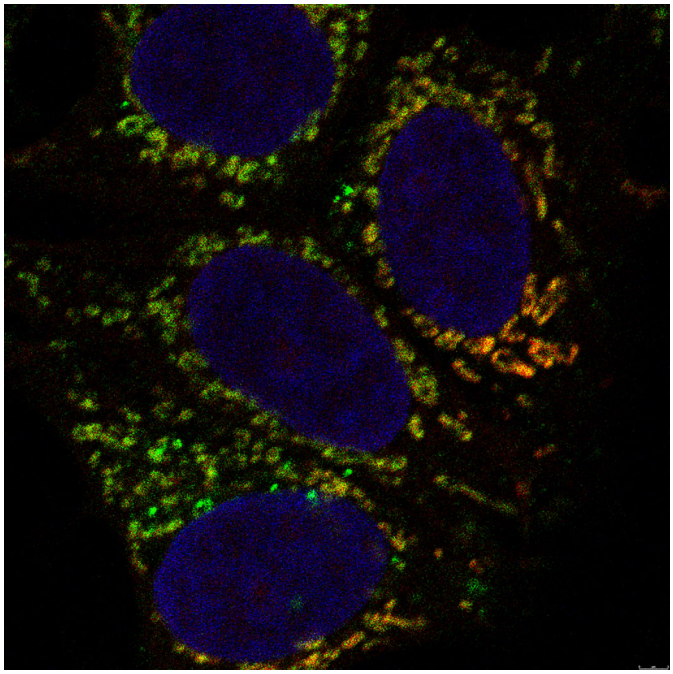
My supervisor, Dr Sanjiban Chakrabarty, supported me throughout the study. Since we both started our career together, by being his first PhD student, we built this project from scratch. Along the way, we faced failures and cherished success together. This article is very special for him as well, being his first corresponding author paper. He always said the student is the one who drives the project, and the supervisor is the driving force behind it.

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?

My inclination towards biology started during my master's project semester when I was studying the virulence properties of bacteria. However, I had a change of heart eventually towards cell biology and wanted to learn more about various cellular pathways that are

Raviprasad Kuthethur's contact details: Manipal School of Life Sciences, Manipal Academy of Higher Education, Planetarium Complex, Eshwar Nagar, Manipal, Karnataka, India 576-104
E-mail: raviprasad.kv@learner.manipal.edu. Twitter: @RaviprasadKV1

Journal of Cell Science (2022) 135, jcs260115. doi:10.1242/jcs.260115



Immunofluorescence imaging of mitomiR-5-5p localization inside the cells. Biotin-tagged mitomiR-5-5p mimic was counterstained with MitoTracker Red and DAPI.

altered during cancer progression. During this study, I got introduced to mitochondria and their multiple functions that get changed in a cancer cell.

Who are your role models in science? Why?

Many scientists have dedicated their lives to the pursuit of excellence in science. Among them, I was always fascinated by the work of Sir C. V. Raman, whose work inspired me to study science during my graduation years. I am also a great admirer of Marie Curie and am inspired by her life and achievements despite significant adversity.

What's next for you?

As I'm approaching the end of my PhD program, I would like to pursue post-doctoral research and become an independent researcher to achieve my goals.

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

I love traveling and exploring new places. I am also a foodie and love cooking.

Reference

Kuthethur, R., Shukla, V., Mallya, S., Adiga, D., Kabekkodu, S. P., Ramachandra, L., Saxena, P. U. P., Satyamoorthy, K. and Chakrabarty, S. (2022). Expression analysis and function of mitochondrial genome-encoded microRNAs. *J. Cell Sci.* **135**, jcs258937. doi:10.1242/jcs.258937