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FIRST PERSON

# First person – Srinivas Animireddy

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. Srinivas Animireddy is first author on 'Aberrant cytoplasmic localization of ARID1B activates ERK signaling and promotes oncogenesis', published in JCS. Srinivas conducted the research described in this article while a PhD student in Dr Murali Dharan Bashyam's lab at the Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad, India. He is now a postdoc in the lab of Dr Blaine Bartholomew at the MD Anderson Cancer Center, Smithville, TX, investigating the role of chromatin remodelers in development and diseases.

Srinivas Animireddy

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

Pancreatic cancer, being the third and seventh leading cause of cancer-related deaths in the USA and worldwide, respectively, is a highly aggressive cancer with poor prognosis. In our study, we propose a novel mode of action of ARID1B, a classical nuclear tumor suppressor protein frequently inactivated in pancreatic cancer. When localized to the cytoplasm, ARID1B appears to activate (and not suppress) pancreatic oncogenesis. Thus, we have identified a 'yin and yang' function of ARID1B based on its dual localization in cells.

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

The most challenging part of the project was expressing and detecting a high molecular weight (280 kDa) protein, which is a typical problem many biologists face. Dr Reiko Watanabe (Tohoku University, Sendai, Japan) was kind enough to provide us with ARID1B and ARID1A clones, which saved us from cloning this huge ORF. It took several months of optimization experiments to transfect and detect protein signals on western blots. We standardized several techniques, including establishing HALO-tag technology and the generation of point mutations. We also tested various reagents for each experiment, such as transfection reagents, vector backbones, cell lines, and a lot of perseverance! Finally, we obtained some intriguing results pertaining to the neomorphic oncogenic function of ARID1B. Another challenge was in quantifying and analyzing the immunohistochemistry images of tissue microarrays of pancreatic and breast cancer used in this paper. We are thankful to our clinical collaborators who supported us in interpreting the data.

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

Previously, we knew the SWI/SNF subunit ARID1B to be a nuclear tumor suppressor, as suggested from our own and others' previous studies. However, we discovered ARID1B localization in the cytoplasm of pancreatic cancer samples but had no clue to its functional significance. Our 'eureka' moment was when we obtained evidence for an oncogenic role of cytoplasm-localized ARID1B. This particular landmark observation set us on the right path that ultimately led to the discovery of ARID1B-mediated regulation of RAF–ERK signaling.

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

JCS is a reputed journal that covers a diverse breadth of research areas in cell biology and has a broad readership. We chose JCS as the best place to publish our data to reach a wide range of the scientific community because of the journal's scope, its proficient editorial board and a quick turnaround time.

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

I am fortunate to have had Dr Murali Dharan Bashyam as my PhD guide. He was always there to support me through thick and thin, and encouraged me to try innovative ideas, guiding me with critical inputs. I would like to recollect that during this journey we faced many hurdles, but he never gave up on the project. His forbearance

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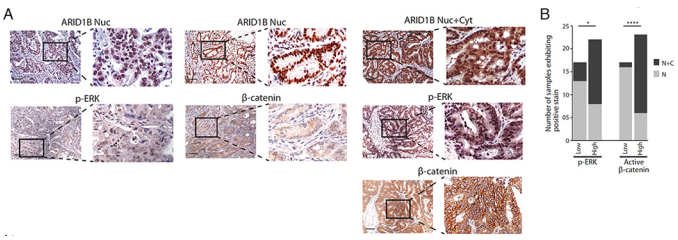


**ARID1B cytoplasmic localization correlates with increased levels of active ERK and β-catenin in human pancreatic tumor samples.** Panel A shows representative immunohistochemistry (IHC) images from samples exhibiting: nuclear ARID1B and weak phosphorylated ERK (p-ERK) staining (left); nuclear ARID1B and weak β-catenin staining (middle); and nuclear plus cytoplasmic ARID1B, strong p-ERK and strong β-catenin staining (right). Panel B shows a graphical representation of the IHC results. N, positive for ARID1B nuclear staining; N+C, positive for ARID1B nuclear plus cytoplasmic staining.

has always led us to achieve more. He has trained me in such a way that my technical as well as scientific skills have drastically improved. I sincerely thank him for everything.

### 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?

During high school, I was fascinated by the process of photosynthesis in plants, which supports the life of everyone by producing oxygen. I believe studying science or scientific research is the key to unraveling such complex biological processes that exist in nature to support the formation and evolution of life. Curiosity to understand such complexity of biological science is what motivates me.

### Who are your role models in science? Why?

It's tough to consider a particular person as my role model because everyone is doing their best to improve knowledge in their respective streams and to serve mankind. So, I adore all the researchers for their dedication to improving human life and thus sharing vast knowledge with the newer generations.

### What's next for you?

I have just started my postdoc career at the MD Anderson Cancer Center. I want to build my research network and gain expertise in cutting-edge molecular biology techniques. Then, I would certainly like to become an independent investigator in the field of epigenetics driven by chromatin remodeling complexes and their importance in diseases.

#### Reference

**Animireddy, S., Kavadipula, P., Kotapalli, V., Gowrishankar, S., Rao, S. and Bashyam, M. D**. (2021). Aberrant cytoplasmic localization of ARID1B activates ERK signaling and promotes oncogenesis. *J. Cell Sci* **134**, jcs251637. doi:10.1242/jcs.251637