

FIRST PERSON

First person – Ahmed Abdelbaki Abdelaal and H. Begum Akman

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. Ahmed Abdelbaki Abdelaal and H. Begum Akman are co-first authors on 'AURKA destruction is decoupled from its activity at mitotic exit but is essential to suppress interphase activity', published in JCS. Ahmed is a PhD student, and Begum a Research Associate, in the lab of Catherine Lindon at the Department of Pharmacology, University of Cambridge, UK, where they are investigating the contribution of ubiquitin-mediated signaling to the outcomes of cell division.

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

A.A.A. and H.B.A.: Cell division is the basis of life itself and is required for the growth and replacement of damaged cells. Uncontrolled cellular division means cancer. Therefore, it is very important to study how cells divide and how daughter cells reorganize after division. Mitosis is a type of cell division where genetic materials (the blueprint of a cell), as well as cytoplasm and organelles (the building blocks), are equally segregated between the daughter cells to ensure their viability. Therefore, cells have evolved different mechanisms and pathways to enhance the accuracy of mitosis and cellular reorganization. After cell division, the daughter cells reorganize the mitochondria (the powerhouses of the cell) into a functioning network. These events are generally controlled by the activation, inactivation and destruction of protein kinases and phosphatases. In this article, we focused on the regulation of Aurora A kinase (AURKA), a key regulator of the cytoskeleton and of mitochondrial fragmentation during cell division. In normal cells, AURKA is destroyed at the end of mitosis. We used genome editing to make cells incapable of destroying AURKA. Interestingly, we found that destruction is not required for AURKA inactivation at the end of mitosis but is required during interphase. If destruction is blocked, mitochondria appear more fragmented in interphase. Blocking AURKA activity by drug treatment allows the mitochondria to reassemble after mitosis.

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

A.A.A.: Finding reliable tools for measuring AURKA activity was a major challenge in our study. AURKA activity is regulated by phosphorylation on its activation loop as well as interaction with its binding partners. Therefore, using a phospho-antibody alone as a marker for AURKA activity might be misleading for the true kinase activity. For this reason, we decided to collaborate with Olivier Gavet's lab who were developing a new FRET biosensor, which is more reliable and enables us to measure the dynamics of AURKA activity in living single cells.



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H.B.A.: Having a knockout model to study function and downstream effects of a protein is very advantageous in research. The most challenging part was to generate an FZR1^{KO} line using CRISPR technology. The gene structure of FZR1 is not ideal for genome editing; to overcome this problem I tried several guide RNAs and screened lots of clones to find successfully deleted ones.

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

A.A.A.: I was observing the activity of AURKA in the absence of its destruction, using FRET imaging. It was very surprising to see that although AURKA protein levels were constant, kinase activity dropped during mitotic exit and went up again in interphase. That was an amazing and unique solution for cells to exit mitosis without errors, but how cells switch AURKA off and on was a question that stuck in my mind. Observing the mitochondrial fragmentation in cells overexpressing AURKA was another striking moment to me.

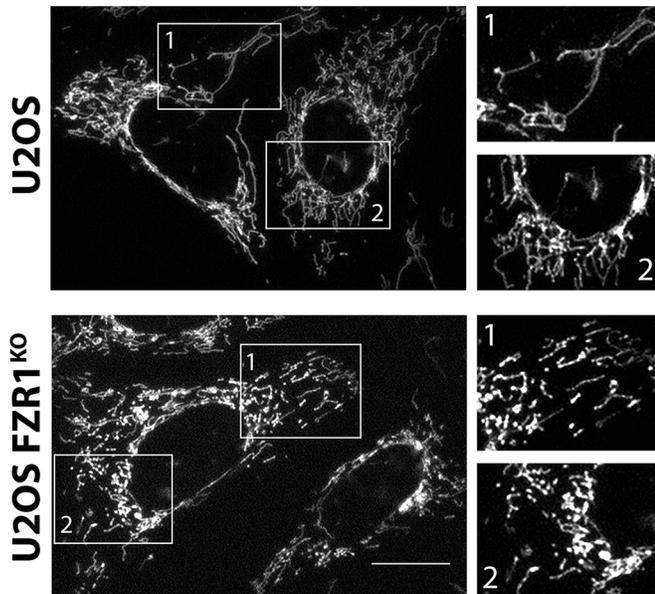
H.B.A.: I generated the FZR1^{KO} cell line as a model to study and better understand the contribution of APC/C–FZR1 substrates to cell fate in the following interphase. When I first started working with these cells, although an increase in AURKA levels was expected, the 'eureka' moment came when we first observed western blots showing that the activity of AURKA is decoupled from its levels at mitotic exit. Ahmed was already interested in the destruction/inactivation dynamics of AURKA and its interphase functions, so this evidence from FZR1^{KO} cells encouraged us to continue working together on this project.

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

A.A.A.: Our paper matches the aim and scope of Journal of Cell Science.

H.B.A.: Journal of Cell Science is a journal from a not-for-profit publisher and a very well-recognized journal in the cell biology field.

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Mitochondria are over-fragmented in interphase FZR1 knockout cells compared to the parental U2OS cell line. Scale bar: 10 μ m.

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

A.A.A.: My parents and my supervisor have always been supportive and encouraged me to work hard throughout my studies. My supervisor has guided me to becoming an independent researcher. I learned so much from her expertise in the field.

H.B.A.: I have been lucky to work with and learn from two strong female PIs. My PhD supervisor Dr Elif Erson-Bensan always encouraged me to pursue new questions, and she taught me a lot about how to be resilient in science. During my postdoctoral research, Dr Catherine Lindon has been the most supportive PI during my transition to the cell biology field. Her guidance throughout my research taught me to be more creative and ambitious in pursuit of my scientific goals.

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?

A.A.A.: I chose to pursue a career in science because I am curious to understand how and why things happen the way they do. In my opinion, there is nothing more enjoyable than searching for

knowledge. The most interesting moment in my life was getting a USAID fellowship to study for a master's degree in the USA. It was a turning point for me as it gave me the chance to learn how to do science first-hand. It was very hard at the beginning, but I quickly adapted and learned from this great opportunity to carry out research and how to do experiments and build ideas.

H.B.A.: I have always enjoyed acquiring knowledge and solving problems. Science brings these two together and gives you the freedom to ask new questions. I think as cell biologists we are trying to find the pieces to solve the big jigsaw puzzle, and I love jigsaw puzzles!

Who are your role models in science? Why?

A.A.A.: Ahmed Zewail is my role model in science. He was the first Egyptian and the first Arab to receive a science Nobel Prize. He invested time to motivate and encourage young people to pursue a career in science. I also look up to Conly Rieder; he was for many years a world leader in the field of mitotic cellular division.

H.B.A.: I admire scientists who are not only experts in their fields but also advocates of science by pursuing public engagement. I believe participation in science outreach is a very crucial part of being a scientist.

What's next for you?

A.A.A.: I am planning to find a postdoc position so that I can pursue my research interests while training students in the lab to solve relevant problems.

H.B.A.: I am aiming to find an academic position in my home country, Turkey, to lead my own research team.

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

A.A.A.: I like watching football games. My favourite team in England is Liverpool. I wait eagerly for weekends when I can watch Liverpool play.

H.B.A.: I like playing video games. I have been a gamer for a long time and I prefer MMORPGs. I am a guild master in a game – I know most of the people in the guild and even became friends with some of them in real life! I think playing games helps me reduce my stress when times are challenging in the lab.

Reference

Abdelbaki, A., Akman, H. B., Poteau, M., Grant, R., Gavet, O., Guarguaglini, G. and Lindon, C. (2020). AURKA destruction is decoupled from its activity at mitotic exit but is essential to suppress interphase activity. *J. Cell Sci.* **133**, jcs243071. doi:10.1242/jcs.243071