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FIRST PERSON

First person – Tigist Tamir

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. Tigist Tamir is first author on 'Gain-of-function genetic screen of the kinome reveals BRSK2 as an inhibitor of the NRF2 transcription factor', published in JCS. Tigist conducted the research described in this article while a graduate student in Michael Ben Major's lab at Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, USA. They are now a postdoctoral associate in the lab of Forest White at Koch Institute for Integrated Cancer Research, Massachusetts Institute of Technology, Cambridge, MA, where they are interested in integrating cutting edge 'omics' technologies to better elucidate drivers of cancer progression and therapy resistance.

Tigist Tamir

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

In the process of life, cells often generate metabolic waste in the form of oxidative damage that is detrimental for survival. Therefore, cells have evolved pathways to breakdown, neutralize or eject noxious molecules through a well-orchestrated antioxidant response. One of the major regulators of antioxidant response is the transcription factor nuclear related factor-erythroid 2 like 2 (NRF2). Changes in NRF2 levels are a key feature of a number of human diseases, including, but not limited to, cardiovascular diseases, neurodegenerative disorders and cancer. Since directly targeting NRF2 in human disease has presented a challenge, we sought to evaluate other targetable signaling hubs. That is when we evaluated kinases, because they are easier to target with small-molecule inhibitor drugs, and a number of kinase inhibitors are used in clinical trials for new drugs. Using a large-scale screening technique, we identified the kinase BRSK2 as a new regulator of NRF2 and a potential candidate for drug design in stress-related disease.

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

After identifying that BRSK2 reduced NRF2 at the protein level, showing how BRSK2 blocks protein translation was technically challenging. In order to address this, we tracked changes in ribosome–mRNA binding using polyribosome profiling. These results along with our 'omics' data showed that BRSK2 significantly reduced the rate of protein translation. These findings also underscore the importance of the collaboration in science. Our work was strengthened by the collaborative work done with Dr Nathaniel Moorman and his graduate student Andrew Hale, who lent their expertise in the field of protein translation biology.

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

Yes, the majority of NRF2 regulation happens at the protein degradation step. But BRSK2 was not linked to degradation, which posited a potential mechanism I had not considered. This led to further investigation that showed that BRSK2 plays a role in protein synthesis, thus moving the regulatory step away from degradation. Because of this finding, I explored the connection between cellular stress, metabolism and the speed of stress response that I continue to pursue today.

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

The eclectic nature of the story and the focus on cell signaling was a great fit for JCS.

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

My thesis advisor Dr Ben Major encouraged and supported me to explore the breadth of the project as the story evolved into topics, which led to numerous collaborations that helped us answer many questions. Additionally, Dr Michael Emanuele, who was on my thesis committee, has made time for invaluable discussion that gave me an opportunity to think outside the box throughout this study. The contributions of scientific discussion might not be as apparent in published work, but are essential in helping us get to the answer.

Who are your role models in science? Why?

Dr Aklilu Lemma is one of my scientific heroes. He was an Ethiopian scientist who discovered a natural remedy for schistosomiasis from the berries of the Endod (*Phytolacca dodecandra*) plant. Growing up in Ethiopia, I was taught about his work in my science classes, and he

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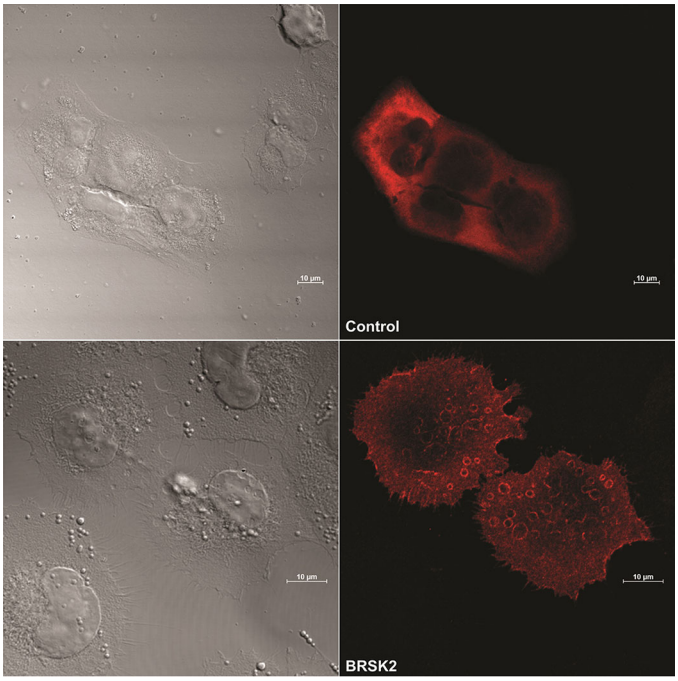

Induction of vesicles in cells overexpressing BRSK2. These vesicles are outlined by BRSK2 protein (red).

was inspiring because his discovery lead to various scientific works on plant remedies for diseases caused by parasites. In addition, his work in UNICEF, and subsequent work to incorporate research into the everyday life of Ethiopian public, made me want to make the world a better place through science.

What's next for you?

I am pursuing post-doctoral studies with Dr Forest White at MIT, where I am focusing on studying kinase-regulated metabolic signaling in cancer.

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

Throughout graduate school, I dealt with the stress of everyday failure by taking up Tae Kwon Do. It was a wonderful way to de-stress, and provided me with useful skills that helped me to stay focused. Unlike my experiments, Tae Kwon Do gave me achievable goals that come with hard work, and put lab failures into long-term perspective. Often in graduate school, we tend to be unkind to ourselves due to the day-to-day toil, and it is important to remember that we can harness the success of other aspects of our life to stay in the game.

Reference

Tamir, T. Y., Bowman, B. M., Agajanian, M. J., Goldfarb, D., Schrank, T. P., Stohrer, T., Hale, A. E., Siesser, P. F., Weir, S. J., Murphy, R. M. et al. (2020). Gain-of-function genetic screen of the kinome reveals BRSK2 as an inhibitor of the NRF2 transcription factor. *J. Cell Sci.* **133**, jcs241356. doi:10.1242/jcs.241356