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FIRST PERSON

First person – Xiaoyun Li

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. Xiaoyun Li is first author on 'Mechanisms of malignancy in glioblastoma cells are linked to mitochondrial Ca^{2+} uniporter upregulation and higher intracellular Ca^{2+} levels', published in JCS. Xiaoyun is a PhD student in the lab of Vincent Torre at the Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy, investigating the mechanisms of malignancy associated with intracellular calcium levels in glioblastoma cells.

Xiaoyun Li

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

Glioblastoma (GBM) is one of the most malignant brain tumours, and despite advances in treatment modalities, it remains largely incurable. In our study, we found glioblastoma cells are characterized by spontaneous calcium waves reaching unusual levels, during which the intracellular calcium concentration reaches values above 1–3 µM which is much higher than in human astrocytes (HAs). This is a surprising observation, which – to our knowledge – has never been made before. The mitochondrial calcium uniporter (MCU) in glioblastoma cells is upregulated. Here, we show that MCU silencing decreases proliferation and alters intracellular calcium dynamics in U87 GBM cells, while MCU overexpression increases calcium elevation in HA. These results suggest that changes in the expression level of MCU, a protein involved in intracellular calcium regulation, influences glioblastoma cell proliferation, contributing to glioblastoma malignancy. Targeting the MCU complex and intracellular calcium regulation could be a new unexplored strategy for the treatment of glioblastoma.

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

The most challenging part was to quantify the calcium concentration in live cells. We used ratiometric calcium imaging based on two calcium indicators, Fluo-4 AM and Fura Red AM. In our lab, we had experience in normal calcium imaging experiment but no experience in ratiometric calcium imaging. It took us quite some effort to optimize live-cell imaging settings and set up assays. To ensure the reliability of the results, the experiment details were strictly controlled, such as exposure time, dye concentration, incubation time, cell density and culture time. These standardizations made it possible to quantify the real intracellular calcium concentration and track calcium dynamics in live cells.

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

We compared the intracellular calcium and MCU expression level in HAs and GBM cells, and found that both intracellular calcium and MCU expression are higher in GBM cells. MCU knockdown in U87 GBM cells indicated that a decreased MCU level was accompanied by decreased intracellular calcium level and cell proliferation. MCU overexpression in HAs showed increased MCU levels and increased intracellular calcium levels, but reduced cell proliferation. After cell death analysis, the 'eureka' moment came. MCU overexpression in HAs slightly increased calcium level but causes cell death, suggesting that HAs cannot tolerate high MCU levels.

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

Journal of Cell Science has a good reputation and is very high level in the cell biology field. We choose Journal of Cell Science to publish our paper because we want to reach a broad audience of cell biologists. Additionally, the publication system of this journal is user-friendly.

Have you had any significant mentors who have helped you beyond supervision in the lab?

I would like to take this opportunity to specially thank Professor Vincent Torre for his continuous guidance and support during my whole PhD period. He has a constant passion for science and has always encouraged me to try new ideas. Several aspects of this project were challenging and it was not easy to perfectly interpret the results. With Professor Torre's professional suggestions and encouragement, I overcome all these difficulties. He is a smart and positive person telling me to work hard and also to be creative in my future research life.

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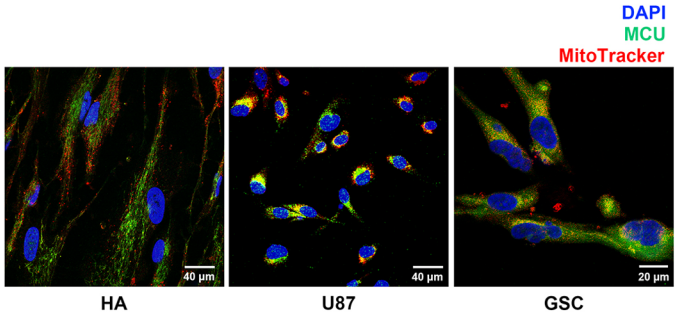

Confocal images showing the expression of MCU in HAs, U87 GBM cells and GSCs from a patient. Co-staining with the mitochondrial marker MitoTracker Red shows a strong colocalization, confirming MCU localization on the mitochondria.

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?

I have loved understanding how things work since I was young, and my mother has always encouraged me to look for answers with a scientific eye. After learning that so many physiological activities can work together so accurately, I was thrilled by how fascinating life is. Brain tumors torture patients and remain largely incurable despite advances in treatment modalities. So when I had the opportunity to do biological research related to brain tumors, I chose it without hesitation.

Who are your role models in science?

I admire female scientists who love scientific research, have achieved success in science, and have happy families.

What's next for you?

I am in the fourth year of my PhD and I will finish my project in the coming year. In the future, I want to look for a position that encompasses therapeutic application and theoretical research, and I hope to make some contribution to brain tumour treatment.

Reference

Li, X., Spelat, R., Bartolini, A., Cesselli, D., Ius, T., Skrap, M., Caponnetto, F., Manini, I., Yang, Y. and Torre, V. (2019). Mechanisms of malignancy in glioblastoma cells are linked to mitochondrial Ca^{2+} uniporter upregulation and higher intracellular Ca^{2+} levels. *J. Cell Sci*. **133**, 237503. doi:10.1242/jcs.237503