

FIRST PERSON

First person – Andri Christodoulou

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. Andri Christodoulou is first author on 'TMEM147 interacts with lamin B receptor, regulates its localization and levels, and affects cholesterol homeostasis', published in JCS. Andri conducted the research described in this article while a postdoc in Professor Niovi Santama's lab at the Department of Biological Sciences, University of Cyprus, Nicosia, Cyprus. She is now a postdoc in the lab of Dr Paris Skourides at the Department of Biological Sciences, University of Cyprus, investigating the role of transmembrane proteins in the morphogenesis and function of the endoplasmic reticulum.

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

Cholesterol is a type of lipid that is extremely important in mammalian cells as part of their plasma membrane and for the synthesis of steroid hormones, vitamin D and bile acids. Cells can obtain cholesterol from the diet and can also synthesise it in their endoplasmic reticulum (ER), their largest membranous compartment. In our work, we studied the protein TMEM147, which localizes to the ER and the nuclear envelope in human cultured cells. We found that TMEM147 physically interacts with the proteins LBR and DHCR7, which are key enzymes catalysing different steps in cholesterol biosynthesis. When we experimentally lowered levels of the TMEM147 protein in cells, we observed a resulting reduction of both LBR and DHCR7 protein levels and gene expression, as well as a mistargeting of LBR from the nuclear envelope to the ER compartment. Functionally, this manifested as changes in cellular cholesterol levels, reduction of the levels and profile of cholesteryl esters (storage forms of cholesterol) and an increase in the ability of cells to take up external cholesterol. All in all, our work indicated that the newly characterised TMEM147 protein might be an important new regulator of cellular cholesterol homeostasis. This is important given the prominent role of cholesterol in health and disease.

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

The biggest challenge that I faced during this project was when we received the reviews from JCS. At that time my country, Cyprus, was under strict lockdown due to the COVID-19 pandemic. Fortunately, the University of Cyprus provided me with special permission to work, and I managed to produce the work needed in the time limit that I had.

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

When I first started to characterise TMEM147 and to understand its role in ER morphogenesis and function, I didn't know what to expect. As the project evolved, I found that silencing of TMEM147 causes reduction in LBR protein levels and mistargeting of LBR from the inner nuclear membrane to the ER. TMEM147 physically



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interacts with LBR, and the C terminus of LBR, which resembles C-14 sterol reductase enzymes, is essential for their functional interaction. Having these results in hand, I knew that I should investigate the role of TMEM147 in cholesterol biosynthesis. After that, things were very clear.

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

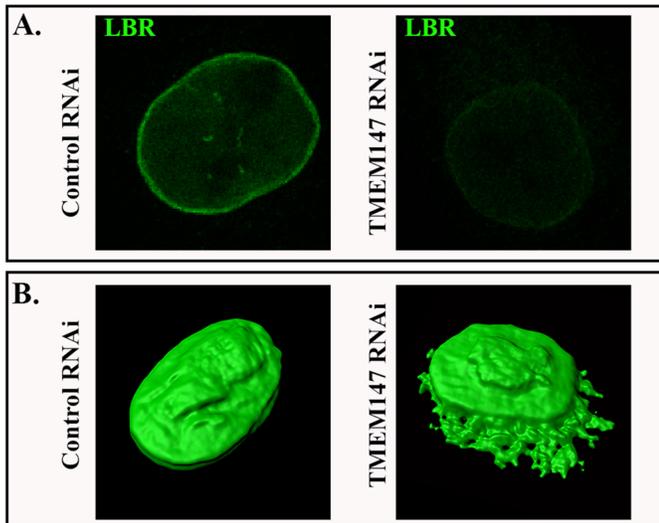
This is not the first time that I have published my work in JCS. I have previously published two other papers in the journal. What I truly like about JCS is that the reviewers are really professional; their comments and the extra work they ask for always improves the quality of my work, and I am very happy with the result. In addition, JCS is one of my favourite journals to read.

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?

From the moment I entered the lab as a PhD student and started to have my first experiences in the field of research, I knew exactly what I wanted to do in my life. I am who I am today as a scientist due to two facts: (1) I had Professor Niovi Santama as my PhD supervisor, who taught me, at my first steps, to set the bar of my work high, to be focused on my goal and to do science with passion; and (2) I did my first postdoc at the European Molecular Biology Laboratory (EMBL), with an EMBO fellowship. There, I joined the lab of Professor Iain Mattaj, and I consider myself very lucky that I had the chance to work under his supervision. I will always be grateful to him that he gave me this great opportunity. Furthermore, working at the EMBL, one of the world's leading research institutions, really broadened my scientific horizons and improved me as a scientist.

Who are your role models in science? Why?

My role models in science are women such as Marie Curie and Rosalind Franklin, whom I admire not only for their great scientific achievements but mainly for the fact that they paved the way for



TMEM147 regulates the localization and levels of lamin B receptor (LBR). (A) Silencing of *TMEM147* drastically reduces the level of LBR at the inner nuclear membrane and results in mistargeting of LBR to the ER. (B) 3D-rendering of LBR distribution.

women in science. These women had the strength to work and excel in the male-dominated world of science, demonstrating that women can be brilliant scientists. They thus opened the road for societies to seek gender balance in sciences, as they do today, by supporting women to stay in scientific careers.

What's next for you?

My journey in science does not end here. There are always new questions that need to be answered, and I am ready for the next challenge.

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

When I am not working, I am enjoying my time with my family. We love excursions to the mountains or by the sea, and sometimes I play electronic games with my two sons since I have to be a cool mum, as they say.

Reference

Christodoulou, A., Maimaris, G., Makrigiorgi, A., Charidemou, E., Lüchtenborg, C., Ververis, A., Georgiou, R., Lederer, C. W., Haffner, C., Brügger, B. et al. (2020). TMEM147 interacts with lamin B receptor, regulates its localization and levels, and affects cholesterol homeostasis. *J. Cell. Sci.* **133**, jcs245357. doi:10.1242/jcs.245357