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FIRST PERSON

First person – Seda Yasa

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. Seda Yasa is first author on 'CLN3 regulates endosomal function by modulating Rab7A–effector interactions', published in JCS. Seda is a PhD student in the lab of Stephane Lefrancois at the INRS, Québec, Canada, investigating the role of CLN proteins in intracellular trafficking pathways to develop novel therapeutic strategies for lysosomal storage disorders.

Seda Yasa

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

The most common form of childhood dementia is Batten disease (also known as juvenile neuronal ceroid lipofuscinosis or JNCL), which is caused by mutations in the *CLN3* gene. Patients usually die before the age of 30. The exact function of the CLN3 protein is unknown, making the underlying pathophysiological mechanism unclear. This protein localizes on endosomal lysosomal membranes and its mutations lead to defects in lysosomal functions, giving rise to material accumulation within the cell, followed by neurodegeneration. Lysosomes can digest materials with a variety of different enzymes, which are trafficked to lysosome by the lysosomal sorting receptors, sortilin and CI-MPR. These cargo receptors shuttle between Golgi and lysosome for enzyme transportation. Our data revealed that CLN3 is required for efficient endosome-to-TGN trafficking of the lysosomal sorting receptors after the first round of enzyme carriage to lysosome. So the receptors can promote another round of enzyme sorting to the lysosome; in this way, the lysosome can digest materials efficiently. In our cells lacking CLN3, the lysosomal sorting receptors cannot be recycled back to Golgi and instead are degraded. We have shown that CLN3 mediates stability of these receptors by regulating the interaction of the retromer effector Rab7, the master regulator of endocytic trafficking. Overall, our data provide a molecular explanation for the phenotypes of this lysosomal storage disorder observed in Batten disease patients.

Were there any specific challenges associated with this project?

Working on a protein, the function of which is barely known, is enough to make a research project challenging, but exciting at the same time. You should form a strong hypothesis to proceed in your research because there are thousands of different types of proteins interacting with one another. And so you might get lost in the heap of information, costing time, energy, money, even self-confidence at times. I feel very lucky to have my academic supervisor always reminding me to unravel the notes one by one. As Rumi said, 'The art of knowing is knowing what to ignore'. And I have realized that the pathway appears as you know what information (or proteins) to ignore in your research.

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There were some other challenges waiting too. I have used a technique called BRET to show specific protein–protein interactions in live cells, which is highly important to check the interactions of a transmembrane protein like CLN3. BRET is so sensitive that I had to prepare a separate transfection complex for each single dot of a BRET curve. Counting the repeat experiments together with all the mutant rescues, I did over 3000 transfections just for the BRET results of this paper (not to mention the ones that failed). Those times, when I was very tired and frustrated, I kept thinking of an old quotation by Ovid, 'Dripping water hollows out stone, not through force but through persistence'. I believe this sentence is remarkable, reminding me of the power of persistence, hope, and veracity on the way of scientific advancement.

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

Whenever I repeat my experiments and reproduce the same result, and see that the change is significant!

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

Because the Journal of Cell Science provides good visibility for our work through a not-for-profit organization with a very strong reputation in cell biology. Also, since our lab has published in JCS before, we knew that it has excellent quality editors together with fair and constructive reviews.

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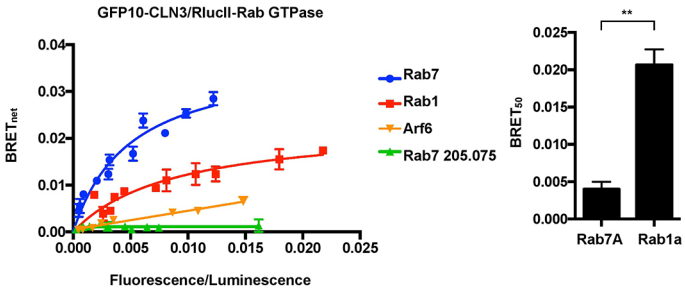

CLN3 interacts with Rab7A.

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

Of course! Although every research article needs a lot of hard work, it may not reach any significance unless you have a great mentor. In this regard, I thank Professor Stephane Lefrancois for being a fantastic supervisor in all respects. I remember the ugliest western blot I had in the first week of my PhD. I said, 'Stephane, do not worry, I will solve this problem'. He calmly looked at me and said, 'I am not worried, I know you can'. He has been not only providing me with a healthy work environment, but also sharing his extensive knowledge, so I have been able to improve my scientific skills. I have to say that I keep on learning a lot from this visionary scientist!

Second, I would like to thank my mother in science Professor Nesrin Ozoren. As a master's student in her lab, I learned how to become an independent scientist with respect to designing and conducting experiments with a diverse set of experimental protocols and techniques. I would also like to mention and thank Professors Ufuk Gunduz and Yusuf Baran, as they have also supported me and given me the lab environment to start my first steps on the way of being a scientist.

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 always been drawn to science and a scientific career. When I was little, I remember being fascinated by people who were wearing lab coats and doing 'science' by mixing things in their flasks and creating solutions to problems addressed by humanity. I remember trying to set up my own mini lab at home with whatever I could find around me and conduct some imaginary experiments. I think that my natural curiosity led me to begin my career in science. My passion and willingness to learn more on these topics still go on.

What's next for you?

After I complete my PhD I want to continue my research career as a postdoc in a lab where I can learn different techniques and technologies.

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

I consider myself a very lucky person. The best example is having my best friend, Furkan Ercan, a successful PhD candidate, as my husband. Apart from that, I used to play piano and do fencing when I was in Turkey. Since I moved to Canada, I draw and skate occasionally. I participate in table tennis tournaments at scientific conferences, and I have always won so far!

What's the most important piece of advice you would give to PhD students?

Compete with yourself, not with others. Find your inner motivation. Do science for humanity, not only for a publication. Pursuing a PhD forms a lifestyle, so be aware of your regular and work habits. And a final piece of advice: work hard, play hard!

Reference

Yasa, S., Modica, G., Sauvageau, E., Kaleem, A., Hermey, G. and Lefrancois, S. (2019). CLN3 regulates endosomal function by modulating Rab7A–effector interactions. *J. Cell. Sci.* **133**, jcs234047. doi:10.1242/jcs.234047