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FIRST PERSON

First person – Cláudia Barata-Antunes and Gabriel Talaia

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. Cláudia Barata-Antunes and Gabriel Talaia are co-first authors on 'Interactions of cytosolic tails in the Jen1 carboxylate transporter are critical for trafficking and transport activity', published in JCS. Cláudia is a PhD student in the lab of Sandra Paiva at Centre of Molecular and Environmental Biology, University of Minho, Campus de Gualtar, Braga, Portugal, where her research interests focus on the study of nutrient transporters endocytosis and trafficking in yeast. Gabriel is a postdoc in the lab of Shawn Ferguson at Department of Cell Biology, Yale University School of Medicine, New Haven, USA, investigating endocytic trafficking and the function of transmembrane proteins and lysosomal signaling in neurodegenerative disorders.

Cláudia Barata-Antunes

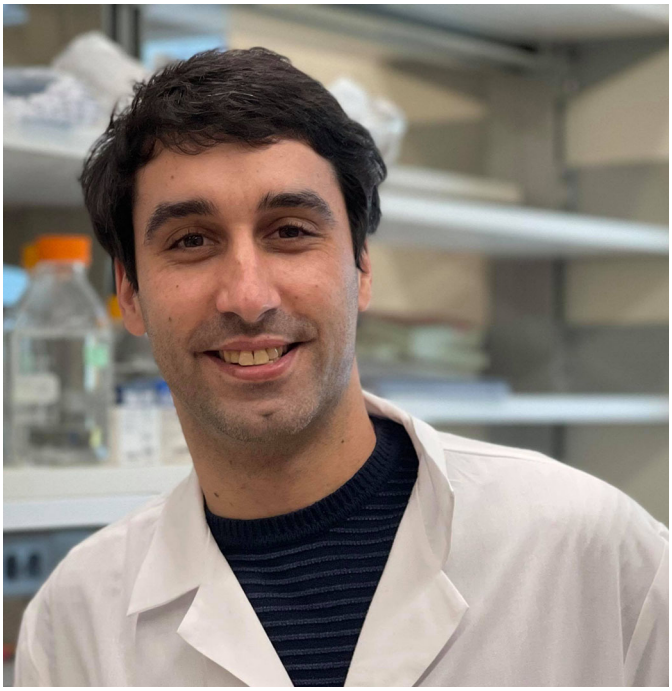
How would you explain the main findings of your paper in lay terms?

C.B.-A.: The yeast *Saccharomyces cerevisiae* has different strategies to balance its metabolism in a changing environment. The removal of specific nutrient transporter proteins (that function as 'gates' for the entry of nutrients) from the plasma membrane (PM) of yeast cells is one of the mechanisms to avoid the uptake of unwanted nutrients or toxic compounds. The process of uptake is called endocytosis and is tightly regulated, involving multiple cellular signaling pathways and the recruitment of adaptor proteins. Our study focuses on the analysis of the nutrient lactate transporter Jen1 in *S. cerevisiae*, more specifically, on how the termini (initial and ending tails) of this transporter affect its localization in the cell, its glucose-induced endocytosis and its affinity for transporting lactate. We found novel roles of the cytosolic termini of Jen1 in its biogenesis, PM stability and transport activity. We also provide evidence supporting the idea that physical interactions between Jen1 termini control these processes.

G.T.: The transport of nutrients and other molecules across the PM is essential for cell adaptation and growth. This process requires PM transmembrane proteins that facilitate their transport, such as transporters, channels or pumps. In this work, we studied the unstructured terminal domains (or simply tails) of a PM lactate transporter, Jen1. We obtained evidence supporting a crucial role for Jen1 tails in transporter function, stability and regulation.

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

C.B.-A.: One of the challenges associated with this project was to find the best growth conditions to express our transporters, at an optimal level, under the control of an inducible system. Another challenge was to define the limits of the Jen1 N- and C- termini as they lack an experimentally defined structure. In the initial stages, we selected longer termini deletions that led to endoplasmic reticulum (ER) retention and non-functional truncated versions of Jen1. Later, the use of AlphaFold helped us understand our first results, which also demonstrate the potential of using this program



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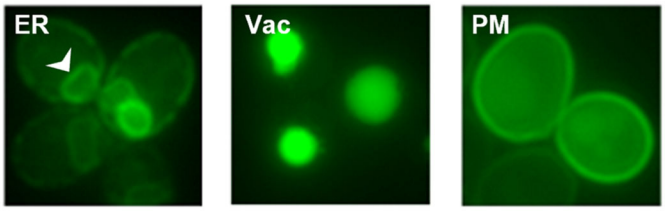

Live-cell imaging of Jen1 transporter mutants in yeast cells. Left, a C-terminal Jen1 mutant (large deletion) causes major ER retention. Middle, an N-terminal Jen1 mutant is constitutively targeted to the vacuole for degradation. Right, a C-terminal Jen1 mutant (small deletion) is highly stabilized at the plasma membrane.

to accurately predict the 3D structure of proteins using their amino acid sequence.

G.T.: One of the major challenges was to find the right tools to study the role of transporter tails. First, we tried to completely delete them, but this led to major trafficking defects of Jen1, with it being retained intracellularly at the ER. This was overcome by deleting smaller parts of Jen1 tails.

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

C.B.-A.: The biggest 'eureka' moment for me was when we discovered that deleting specific shorter segments of the Jen1 termini led to transporter versions with higher affinities (up to a 10-fold increase) for lactate (its natural substrate) as well as an increase in the stability of Jen1 at the PM, even in the presence of glucose, a condition that normally leads to Jen1 endocytosis and degradation. This finding is of particular interest for biotechnological applications and can be exploited for other membrane transporters with the aim of increasing the production of a variety of substrates of interest.

G.T.: A particular result that caught my attention was the high stability of the Jen1 transporter when its C-terminal tail was deleted. This result was important to establish that the absence of tails in Jen1 transporter can be a gain-of-function in relation to stability.

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

C.B.-A.: We chose the Journal of Cell Science because of its prestige with recognized and high-quality scientific papers. The journal addresses a variety of topics in cell biology, reaching a broad audience. I believe that our work will benefit from being published in this journal.

G.T.: Journal of Cell Science is a historical and prestigious journal that publishes great science, so I believe it was the right choice.

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

C.B.-A.: I can say that I had/have two mentors. First, my PhD supervisor, Prof. Sandra Paiva, who always inspired me to be critical and work hard to reach my dreams and goals in science. Her constant motivation and incentive are also associated with a lot of humanity and understanding, which was very helpful in managing the frustrating moments when I was not getting the expected results. My second mentor is Dr Rosana Alves, a post-doc in my lab, who was always there to help me and to inspire me to be a better scientist. With my two mentors I learnt that science is much better when shared and when we work together as a team.

G.T.: Luckily, I have had very significant and brilliant mentors. They have guided me in science and life, helping in the development of my professional, social, and personal skills.

"…I learnt that science is much better when shared and when we work together as a team."

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?

C.B.-A.: My favorite subjects in primary and high school were always science and biology. I felt curious about these topics more than the others and studying them was never boring to me. So, this constant curiosity to learn more and more in these fields led me to pursue a career in science, which is also part of the reason I chose to do a PhD. What motivates me in this path is that we are continuously doing and learning different things, trying to solve new problems and answering new questions.

G.T.: Contributing to the science community with exciting new discoveries is the major driving force that motivates me to continue in science. The most interesting moments in my scientific career are the process of discovering something new, sharing your research data, networking and publishing.

Who are your role models in science? Why?

C.B.-A.: Marie Curie is one of my role models in science. She was the first woman to win a Nobel Prize (twice no less). In a time when it was hard for women to do science, her fundamental research on radioactivity was a major contribution to the progress and development of science and medicine, and she paved the way for other female scientists. I think she is an icon and an inspiration for scientists and women in general.

G.T.: I consider my PhD supervisors Sandra Paiva and George Diallinas and my actual PI Shawn Ferguson to be the most relevant role models in science for me. They are excellent mentors and the way they think about science is unique and exciting.

What's next for you?

C.B.-A: After I finish my PhD, I am planning to continue in academia and apply for a post-doc position in a related research topic. If possible, I would also like to mentor and supervise students in the lab, and share my knowledge and experience with them.

G.T.: Currently, I am a postdoc at Yale University and I expect to continue in academia.

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

C.B.-A.: Besides my love for science, I have a passion for dance. During my free time I do ballet and jazz dance and sometimes I also release my emotions and stress through the writing of poems.

Reference

Barata-Antunes, C., Talaia, G., Broutzakis, G., Ribas, D., De Beule, P., Casal, M., Stefan, C. J., Diallinas, G. and Paiva, S. (2022). Interactions of cytosolic tails in the Jen1 carboxylate transporter are critical for trafficking and transport activity. *J. Cell Sci.* **135**, jcs260059. doi:10.1242/jcs.260059