

## FIRST PERSON

# First person – Susana Peralta

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. Susana Peralta is the first author on 'ATAD3 controls mitochondrial cristae structure in mouse muscle, influencing mtDNA replication and cholesterol levels', published in Journal of Cell Science. Susana is a Senior Research Associate in the lab of Carlos T. Moraes at the University of Miami Miller School of Medicine, Miami, USA, investigating mitochondrial biology and mitochondrial diseases.

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

Mitochondria are very important organelles within cells because this is where most of the energy that our body needs is produced and where many crucial metabolic reactions take place. Mitochondria have two membranes. The inner membrane, which is larger than the outer membrane and is folded in on itself numerous times, contains the enzymatic machinery to produce energy. The folding allows for a larger surface area to maintain the energy-generating enzymes and, in this way, to increase its metabolic capacity. The folds are called cristae. It has been estimated that around a thousand proteins are needed for the correct functioning of the mitochondria. ATAD3 is a mitochondrial protein whose precise function is not known. Mutations in the gene that encodes the ATAD3 protein cause very severe neurological syndromes in humans. To understand the function of ATAD3 in live cells, we have created and characterized a mouse model lacking the ATAD3 protein in the skeletal muscle. We found that the lack of ATAD3 in muscle disrupts mitochondrial cristae organization, altering the assembly of the organization complex that is required to maintain cristae junctions and for the formation of contact sites between the inner and outer membranes. Disruption of cristae organization led to secondary defects in mitochondrial DNA replication, mitochondrial fragmentation and altered cholesterol levels. These findings underscore a primary role of ATAD3 in mitochondrial cristae organization in mammals.

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

When analyzing the COX and SDH *in situ* stain in frozen muscle sections, I found the presence of fibers containing cores devoid of stain. It was challenging in the sense that I had to repeat the experiment many times to truly believe it was not an artifact due to the freezing process or other technical issues during the staining process. Once I was confident that it was not an artifact and it was a reproducible feature, I did an extensive search of old literature that tends to have more descriptive analyses of findings. It turns out that central cores devoid of mitochondrial staining have been observed in muscle fibers from patients with an inherited myopathy, named central core disease. This disease is associated with mutations in ryanodine receptor 1, a protein involved in Ca<sup>2+</sup> transport. To my



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knowledge, this is the first time that the presence of central cores has been associated with a mitochondrial myopathy.

**“I did an extensive search of old literature that tends to have more descriptive analyses of findings.”**

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

Yes, when analyzing the assembly of OXPHOS complexes by Blue Native gel electrophoresis and western blotting, I found that the complex that was most affected was complex V (also named ATP-synthase). This result made me think about the relationship of interdependence that exists between complex V and the organization of mitochondrial cristae. From there, I focused on studying the structure of the mitochondrial cristae and the organization of the MICOS complex when the ATAD3 protein was missing.

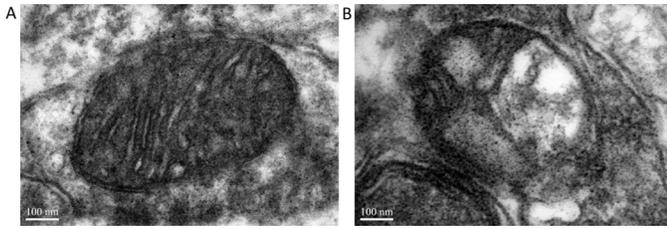
### Why did you choose Journal of Cell Science for your paper?

Firstly, we thought the journal was a good fit because our research is related to basic cell biology. Secondly, because Journal of Cell Science has high standards of scientific rigor.

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

Yes, I am a very lucky person, because all the mentors I’ve had have been great, that’s why I love science! I would like to make a special mention of my current mentor at the University of Miami, Dr Carlos Moraes. His guidance was special in the sense that he makes science seem very easy, and because he cares about the personal aspect of his team. Under his supervision I’ve learned how to ask the right questions, design the proper experiments and interpret the results within that precise context. In addition, I’ve had the opportunity to be mentored by a talented Associate Professor here at the University of Miami,

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Micrographs of mouse brain showing (A) control mitochondria with lamellar cristae, and (B) *Atad3*-knockout mitochondria with disrupted cristae.

Dr Francisca Diaz. She taught me the importance of being rigorous and precise in science, and also that, if you work with passion, the experiments come out much better! I am very grateful to her.

**“[...] if you work with passion, the experiments come out much better!”**

#### Who are your role models in science? Why?

There are many, mostly women. For example, Marnie Falk is a physician and the Executive Director of Mitochondrial Medicine at

the Pediatric Hospital in Philadelphia. She shows excellent dedication and is an excellent speaker. Her ability to connect the work of physicians with basic scientists is remarkable. Also, she is an example of how to have a successful career in science without giving up having a family.

#### What's next for you?

I would love to stay in academia and move back to my country, Spain. Because the opportunities in academia are limited and the economic situation in my country is very complicated, I will not discard the possibility of other options, such as working in pharmaceutical companies.

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

I love to travel. I find it fascinating to discover new countries, their culture and their typical food.

#### Reference

Peralta, S., Goffart, S., Williams, S. L., Diaz, F., Garcia, S., Nissanka, N., Area-Gomez, E., Pohjoismäki, J. and Moraes, C. T. (2018). ATAD3 controls mitochondrial cristae structure in mouse muscle, influencing mtDNA replication and cholesterol levels. *J. Cell Sci.* **131**, jcs217075.