© 2019. Published by The Company of Biologists Ltd | Journal of Cell Science (2019) 132, jcs235952. doi:10.1242/jcs.235952

FIRST PERSON

First person – Carlos Alonso

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. Carlos Alonso is first author on 'MRP4-mediated cAMP efflux is essential for mouse spermatozoa capacitation', published in JCS. Carlos conducted the research described in this article while a PhD student in Dr Silvina Perez Martinez's lab at the University of Buenos Aires, Argentina. He is now a postdoc in the lab of Dr Daniel J. Bernard at McGill University, Montreal, Canada, investigating the molecular mechanisms regulating reproduction at different levels.

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

Freshly ejaculated sperm is not capable of fertilizing the oocyte. Many changes need to occur for the male gamete to gain that ability, and together these changes are known as capacitation. One of those changes is an increase in the concentration of a molecule called cAMP. This rise in cAMP allows many other downstream changes to happen, and the tight regulation of the levels of this signaling molecule is important for capacitation to take place properly. Multidrug resistance protein 4, or MRP4, contributes to the regulation of cAMP concentration in other cell types and tissues by pumping it out of the cell. The presence or the importance of MRP4 had not previously been investigated in mouse sperm, and that's what this work is about. Here, we determined that MRP4 is important for sperm capacitation, since it actively regulates cAMP levels. But we also detected that MRP4 activity is important to indirectly regulate calcium ions (Ca^{2+}), another important signaling molecule. The regulation of Ca^{2+} is crucial for sperm motility and capacitation overall. This was further corroborated by using a mouse genetic model that lacks the principal Ca^{2+} channel of sperm, CatSper.

From a basic perspective, this work helps us to understand how capacitation takes place. Ultimately these findings may allow us to propose new targets for contraception or develop novel therapeutics for the treatment of infertility and subfertility.

Doing science in a third world country is, overall, challenging.

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

Doing science in a third world country is, overall, challenging. While questions, ideas and controls are flourishing all the time, resources are scarce, and learning how to balance this is an extra skill that you need to apply. The main thing you can do to overcome this situation is to collaborate. My PI has established collaborations inside and outside our institution to share reagents, animals and equipment, and I can attest that cooperation was key to carrying out this work.

Carlos Alonso's contact details: Department of Pharmacology and Therapeutics, McIntyre Medical Sciences Building, McGill University, Montreal, QC H3G 1Y6, Canada.
E-mail: caialonso@gmail.com

Carlos Alonso

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

During the completion of this work we had many eureka moments. This project started by characterizing MRP4 in bovine spermatozoa, and moving to a murine model was, initially, a way to confirm results. We were very surprised to find a different role for MRP4 in mouse sperm! From this journey I would pinpoint especially the moment when we incubated mouse sperm with the MRP4 inhibitor in a Ca^{2+}-free medium and did not detect the loss of motility observed in complete medium. I still remember seeing that through the microscope and screaming.

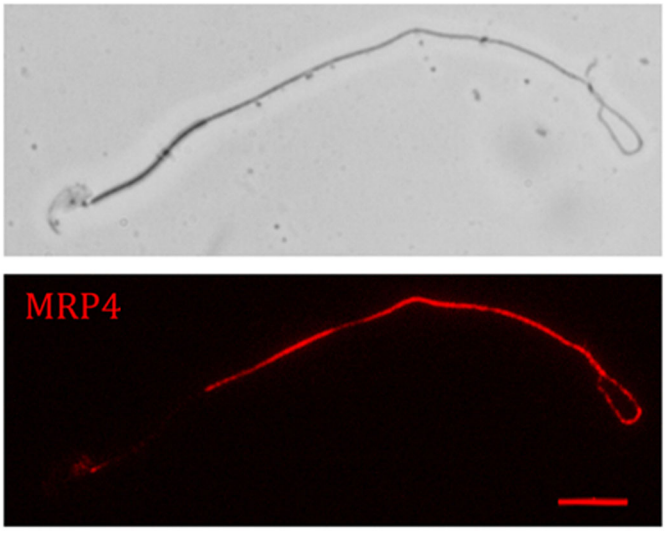
Why did you choose Journal of Cell Science for your paper?

I have some colleagues that have already published in Journal of Cell Science and totally recommended it for its processing times, free-format submission and broad scope. I particularly wanted to submit my work to a general science journal instead of a topic-specific journal to reach a bigger audience and also to test my work in terms of thinking and design in an excellence-driven solid journal. The Journal of Cell Science met this personal criteria and luckily, it worked!

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

I have had two important mentors that helped me during my PhD. The first one was my PI, Dr Silvina Perez Martinez. She always gave me very valuable advice, and supported my ideas while teaching me to be methodical and to work hard. Also her guidance was special because she would help me to think about negative or unexpected

Journal of Cell Science (2019) 132, jcs235952. doi:10.1242/jcs.235952



Mouse spermatozoa immunolabeled with anti-MRP4 antibody. Scale bar: 10 µm.

results, to make the most of them and formulate new hypotheses without getting (too) discouraged. She has a saying inspired by the traditional Argentinian poem called Martin Fierro that reads 'you are not dead if you keep fighting', and I found this applicable to many situations: a tough day in the lab, a rejected application or a bad seminar presentation. My second important mentor was my PhD co-supervisor Dr Carlos Davio. From him I learned that creativity is very important for doing science, and he always gave me the freedom to think of new ways to answer questions or perform experiments. Above all, they are both great people and they always push their mentees to reach their potential. It is easier to keep going when you feel the support of your mentors!

It is easier to keep going when you feel the support of your mentors!

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 remember that as a kid I would watch science-related shows all day (Dexter's Laboratory, Beakman's World or The Magic School Bus). My family saw this and bought me some useful toys like a microscope and a chemistry kit. Many experiments were performed and plenty of insects were examined over time, and when I grew up I always knew that biology was the path to follow. I found great professors and amazing friends at the university where I did my undergraduate studies (University of Mar del Plata), and they all contributed to shaping my career and helped me to take the best decisions to keep pushing my boundaries.

Who are your role models in science? Why?

I admire many scientists, but I always felt the greatest respect for people who can put their work in lay terms and entertain an audience. In that sense, one of my biggest role models is Isaac Asimov. His writings on science popularization are outstanding. His examples are very clear and simple and he knew how to put vast amounts of information (as vast as The Universe) in very easy-to-read text. I am also a sci-fi enthusiast and it is very pleasurable to read his captivating stories about robots, space travel and philosophical dilemmas that are also extremely sound from a scientific perspective.

What's next for you?

I recently finished my PhD and I am planning to continue my research career but in a completely different area. I am engaged in a project with Dr Daniel Bernard from McGill University, in elucidating mechanisms that govern FSH production and release in the pituitary. I think this will allow me to broaden my vision on how to do science, and will give me valuable skills in molecular biology. In the long term, I want to become a professor and start my own laboratory. Just a thought.

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

Last year I accumulated more than 1500 hours of listening to music on Spotify. Most of that time I was either at the desk of my laboratory, reading or writing, or conducting experiments!

Reference

Alonso, C. A. I., Lottero-Leconte, R., Luque, G. M., Vernaz, Z. J., Di Siervi, N., Gervasi, M. G., Buffone, M. G., Davio, C. and Perez-Martinez, S. (2019). MRP4-mediated cAMP efflux is essential for mouse spermatozoa capacitation. *J. Cell Sci.* **132**, 230565. doi:10.1242/jcs.230565