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FIRST PERSON

First person – Nancy Nader

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. Nancy Nader is the first author on 'The VLDL receptor regulates membrane progesterone receptor trafficking and non-genomic signaling', published in Journal of Cell Science. Nancy is a research associate in the lab of Khaled Machaca at Weill Cornell Medical College in Qatar, Doha, Qatar, working on the characterisation of non-classical membrane progesterone receptors and the study of their pathways in different animal and tissue models.

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

The hormone progesterone is known to prepare the oocyte (immature egg) for fertilisation in the African clawed frog by switching it from an 'oocyte' state to 'egg' state in a process called oocyte maturation. In order to perform its action, progesterone initiates a series of consecutive steps by associating with a specific partner protein called the membrane progesterone receptor (mPR), localised at the outer boundary of a living cell, the plasma membrane. The localisation of mPR at the plasma membrane is vital for its function. In this study, we show for the first time that a special protein called VLDLR associates with mPR and acts as a delivery truck that ensures the transit of mPR from the endoplasmic reticulum, which is the main factory for all proteins inside the cell, to the Golgi body, the cellular 'delivery depot' from which proteins are transported to the plasma membrane. In the absence of VLDLR, mPR cannot be delivered to the plasma membrane and so cannot function as a progesterone mediator, and as a consequence the oocytes can no longer mature into eggs ready for fertilisation.

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

The main challenge we faced during this project was a lack of good antibodies raised against *Xenopus* mPR and VLDLR. In order to quantify the plasma membrane localisation levels of endogenous mPR before and after VLDLR knockdown, we used a progesterone analogue coupled to BSA and fluorescein, making it membrane impermeable because of the BSA moiety and allowing easy imaging and quantification of endogenous mPR at the plasma membrane. In order to show that VLDLR antisense oligonucleotides effectively degrade VLDLR protein levels, we overexpressed a VLDLR construct with a C-terminal mCherry tag, with or without a co-injection of VLDLR antisense. We then used the mCherry antibody to detect VLDLR expression on western blots.

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Nancy Nader

"[…] we realised we had a very interesting scientific avenue to explore, and the excitement bulb lit up!"

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

When we first identified VLDLR as a protein that interacts with mPR, we were a bit skeptical since it was a previously unknown and undescribed role for VLDLR. We did not know its significance. However, after knocking down VLDLR expression and finding that it strongly inhibited progesterone-induced oocyte maturation, we realised we had a very interesting scientific avenue to explore, and the excitement bulb lit up! My first of many eureka moments.

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

I chose Journal of Cell Science because of its solid scientific reputation and its relevance to the scientific work we describe in this particular paper.

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

My mentor, Dr Khaled Machaca, plays a solid supporting role in any project I tackle. His guidance is very special because he pushes

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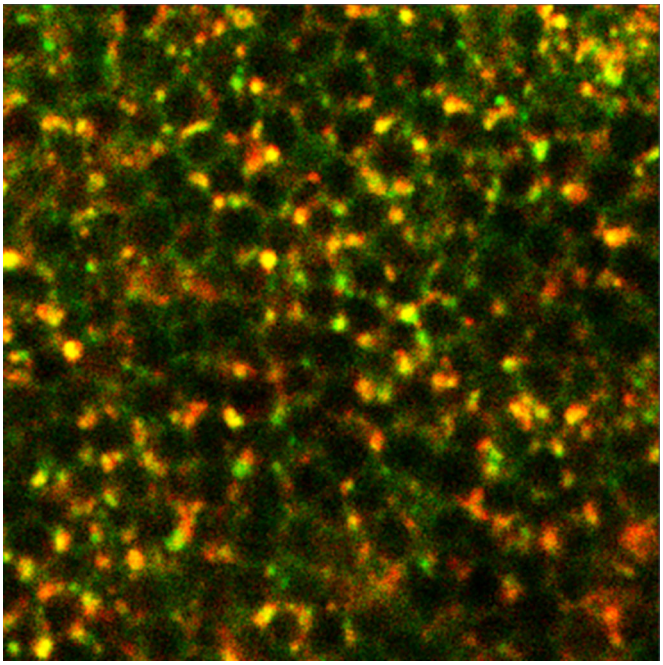

XmPR–GFP and VLDLR–mCherry colocalising in Golgi puncta

me to challenge myself, think outside of the box and be creative when solving problems and trying to find answers to questions.

“[…] every eureka moment I have had with every new project has helped pave the path that led me to where I am now.”

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 am a person who is very fascinated by the human body and its unresolved mystery. I also enjoy problem solving, project management and the act of challenging/proving new hypothesis. Pursuing a career in science and especially in research was a perfect fit for me. My postdoctoral training at NICHD/NIH solidified my love and excitement for research and since then every eureka moment I have had with every new project has helped pave the path that led me to where I am now.

What’s next for you?

I will keep on enjoying the craziness of research and science. My short-term targets are to characterise the membrane progesterone receptor beta and uncover its pathway in oocytes and in different animal and tissue models. My long-term goals are to secure an assistant professor position and ensure funding to keep on building and enjoying my scientific career, and contributing to general scientific knowledge.

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

When I am not doing science, I am either travelling the world, reading, boxing, running, spinning or enjoying time with my family and friends in the presence of good music and delicious food!

Reference

Nader, N., Dib, M., Courjaret, R., Hodeify, R., Machaca, R., Graumann, J. and Machaca, K. (2018). The VLDL receptor regulates membrane progesterone receptor trafficking and non-genomic signaling. *J. Cell Sci.* **131**, jcs212522.