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FIRST PERSON

First person – Jesús Muñoz-Estrada

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. Jesús Muñoz-Estrada is first author on 'Ahi1 promotes Arl13b ciliary recruitment, regulates Arl13b stability and is required for normal cell migration', published in JCS. Jesús is a postdoc in the lab of Ferland Russell at Albany Medical College, Department of Neuroscience and Experimental Therapeutics, NY, investigating primary cilium biology and its association with human diseases.

Jesús Muñoz-Estrada

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

Genes are codes contained in the cell that are translated to proteins, which are biomolecules that the cell and our body require to function properly. The Abelson-helper integration site 1 (*AHI1*) gene encodes for the AHI1 protein and it is located at the base of the primary cilium, a cell organelle that acts as an 'antenna' transmitting extracellular information to the cell. The signals that this cell antenna can interpret includes those of the Sonic hedgehog (Shh) signaling pathway, which is required for proper brain formation. Changes in the *AHI1* gene code can cause a disease called Joubert syndrome (JBTS) and often results in a non-functional protein product. It has been reported that children with JBTS present with malformations of the brain and abnormalities in other organs. However, it is unknown what cell functions are affected when cells are depleted of the protein AHI1, which may explain the organ deficiencies observed in individuals with JBTS, including the brain. In this study, we used mouse cells lacking AHI1 protein to study its function. We found that – consistent with its localization at the base of cilia – AHI1 acts as a 'gatekeeper' regulating movement of the protein Arl13b (another protein associated with JBTS) and also controls the length of this organelle. We also describe that AHI1 controls Arl13b protein stability, the Shh pathway, and cell movement; cell processes that are required for development of the brain and maintenance of tissue function during life. We hope this work contributes to understanding of how AHI1 dysfunction disrupts cellular functions, which may lead to human disease pathogenesis, including JBTS.

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

The major challenge was obtaining AHI1-null mouse embryonic fibroblast (MEF) cultures. The majority of embryos derived from intercrossing *Ahi1*$^{+/-}$ mice (knockout males and females are infertile) were heterozygous for AHI1, suggesting non-Mendelian inheritance. We overcame this challenge by performing more timed pregnancies.

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

A moment of great satisfaction was when we could rescue the ciliary phenotypes observed in cells lacking AHI1 by exogenously expressing AHI1–GFP. We were also surprised by participation of AHI1 in directional cell migration, presumably with no direct involvement of the Pdgfr-α signaling pathway.

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

Because of the outstanding quality and innovation of the work published in the journal. Also, the journal's commitment to advancing the understanding of cell biology.

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

I have been fortunate to have several mentors; what I value the most from all of them is that, first, they have helped me develop critical thinking skills and, second, gave me independence to test several research hypotheses, which have resulted in interesting publications.

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 always curious and eager to learn new technologies that can be applied to generate new knowledge, especially when this knowledge can have direct implications in solving human health problems.

Who are your role models in science? Why?

My role models are my PhD and postdoctoral mentors. They have established and maintained a successful scientific career even though resources for research are increasingly limited.

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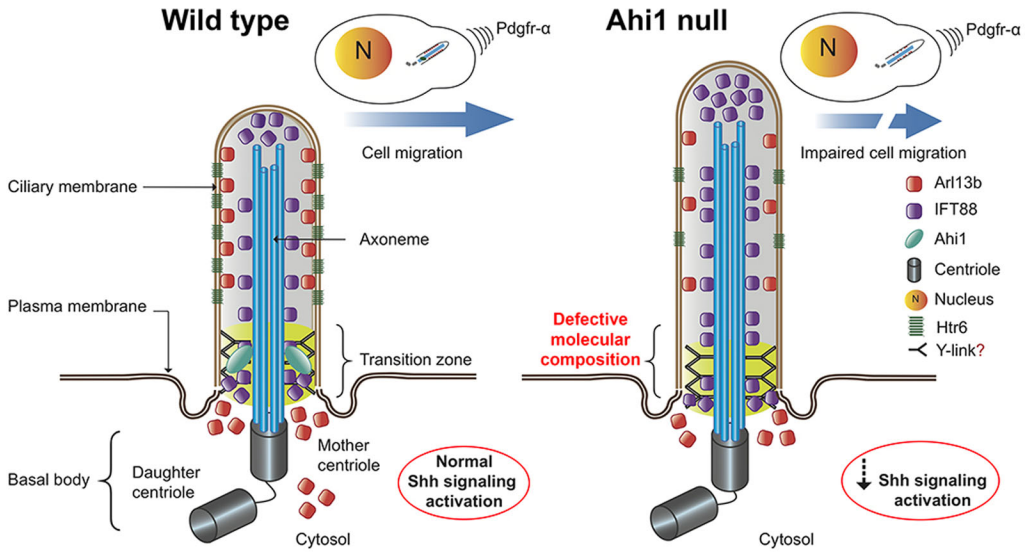

Schematic and simplified representation of the role of AHI1 in cilia and cell function.

What's next for you?

I want to continue my research focusing on primary cilium function and its implications in brain disorders, become an independent researcher, and expand my professional network to establish a bridge between the lab and the clinic.

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

I am passionate about muralism painting, particularly the artistic legacy of Diego Rivera and his contemporaries.

Reference

Muñoz-Estrada, J. and Ferland, R. J. (2019). Ahi1 promotes Arl13b ciliary recruitment, regulates Arl13b stability and is required for normal cell migration. *J. Cell Sci.* **132**, jcs230680. doi:10.1242/jcs.230680