IHS Fellowship report

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Functional validation of microRNAs in migraine-related behaviour in rodent models of chronic migraine

Fellowship from October 2021 to December 2022
Vall d'Hebron Research Institute (VHIR), Barcelona, Spain
Mentor: Patricia Pozo-Rosich

Overview

Clinically, Dr Pozo-Rosich's lab has determined that 2 miRNAs are differentially expressed in migraine patients' serum. The hypothesis is that these miRNAs will be differentially expressed in chronic migraine models in mice, and that their modulation will impact migraine features in behavioural tests (including cephalic allodynia and photophobia) and in *in vivo* electrophysiological tests (including trigeminovascular neuronal activity) in rats. For that, we planned to evaluate 2 miRNA expression in different migraine models including recurrent nitric oxide donor injections and dural application of inflammatory substances, and compare with control group (i.e. wild-type mice). Once an increased expression of these miRNAs is detected, we will inhibit the miRNAs to evaluate their involvement in behavioural tests associated with migraine responses, in comparison with wild-type mice. Thus, the central aim was to functionally validate the involvement of 2 miRNAs in migraine pathophysiology by exploring their functional properties in well-established preclinical models of migraine in rodents.

Summary of research

I am currently working in Patricia Pozo-Rosich's group on the detection of CGRP in saliva. As in the nitroglycerin-induced chronic migraine model, we could not detect CGRP in mice, so we are now investigating the same procedure in rats. Because rats are bigger than mice

and the volume of saliva obtained is greater, we believe we will be able to detect changes in CGRP expression. In addition, we are using another ELISA kit for rats, and adding serum samples as a positive control.

To conduct the research the laboratory space for the preclinical experiments was adapted, as this was a new line of research for the group. The recent literature concerning human and animal models of migraine was reviewed. The research project was approved by the VHIR Ethics Committee on the Use of Experimental Animals. Pilot experiments were done, and the chronic migraine model validated in the lab.

Since the altered miRNAs in migraine patients were not found in mice, we used the opportunity to start an innovative translational project in which CGRP levels in saliva will be monitored during the NTG-induced chronic migraine model in mice. This might help us translate the results obtained in the clinical setting in our group to the chronic migraine model

We did saliva sampling during the NTG-induced chronic migraine model in female mice; saliva was extracted using cotton swabs followed by centrifugation and ELISA for beta-CGRP quantification. Negative results were obtained.

We then did saliva sampling after migraine treatment during the NTG-induced chronic migraine model in female mice. Salivation was induced with pilocarpine and extracted using cotton swabs or micropipette. We had negative results for beta-CGRP.

Finally we did saliva sampling after migraine treatment during the NTG-induced chronic migraine model in female mice. Salivation induced by pilocarpine and saliva extraction using micropipette or cotton swabs. Negative results for alfa-CGRP were obtained.

The altered miRNAs initially found in migraine patients are not orthologous in mice. Therefore, specifically this project could not been translated to the mouse model of chronic migraine.

The review manuscript was written and submitted to a peer-reviewed scientific journal.

Conclusion

The fellowship has allowed me to become a postdoctoral researcher in the field of migraine. I have learned about animal models of migraine and the most relevant molecules for its study,

such as CGRP. In addition, I have learned about the clinical aspect of the disease, which increases my skills for its translational study.

The time spent training in the Migraine Adaptive Brain group will have an important impact in my career. This includes not only the development of new research methodologies, but also the ability to better understand preclinical translational research on headaches and trigeminal pain.

In addition, I was awarded a national postdoctoral research grant to continue my scientific career in Spain (Juan de la Cierva-formación). This ability to demonstrate an early history of external funding, in addition to the novel techniques and scientific knowledge learned during the IHS fellowship, will be essential in obtaining a future research position, which will likely have an exponential impact on my professional career.

For IHS fellowships I recommend looking for groups which already have an established line of research and, if possible, submit projects to the Ethics Committee for approval before the fellowship research begins to avoid delays in starting the project.