Proposal of Master Research Project / Proyecto fin de Master for the academic year 2023-24

Group name: Sensory Transduction and Nociception Group
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Title of the MRP/TFM:
Pain processing at the spinal cord following chemotherapy induced peripheral neuropathy

Summary of the Project:

Chemotherapy induced peripheral neuropathy (CIPN) is a frequent, disabling side effect of anticancer treatments, affecting millions of patients worldwide. The dorsal horn of the spinal cord is the first relay station of cutaneous sensory signals.The molecular identity of the spinal cord interneurons that receive cold and mechanosensitive information, and whether there are alterations in the dorsal horn circuit during CIPN are largely unknown. Thus, the aim of the project will be focused on identifying the spinal neurons that receive inputs from different innocuous and noxious cold and mechanical stimuli in the model of oxaliplatin-induced neuropathy.

Before the development of CIPN, interneurons activated by application of cold and mechanical stimuli in the hindpaw will be permanently marked using the TRAP2-tdTomato mouse line in which cells expressing the neural activity marker c-fos will develop red fluorescence. Next, CIPN will be induced by the injection of the chemotherapeutic agent oxaliplatin and its development monitored using various behavioural tests to assess cold and mechanical sensitivity. Afterwards, additional cold and mechanical stimuli will be applied again and the activated neurons (detected by c-fos immunostaining in spinal cord cryosections) will be compared with the interneurons activated before the CIPN. Additional immunostainings and/or RNA in situ hybridization will be performed in the same sections to elucidate the molecular profile of the activated neurons.

Methods and technology involved in the MRP/TFM Project:

The student will learn to perform histological sections of the spinal cord and immunofluorescence techniques, as well as behavioral tests to evaluate cold and mechanosensitivity. The student will join a multidisciplinary group whose goal is to elucidate the cellular and molecular mechanisms involved in the detection and transduction of physical and chemical stimuli by mammalian sensory nerve terminals, with emphasis on nociceptive terminals. For this purpose we use a wide range of techniques such as molecular biology and genetic manipulation, RNASeq, pharmacology, immunocytochemistry, in vitro and in vivo electrophysiology, piezoelectric activation of mechanosensitive channels, imaging techniques such as intracellular calcium and TIRF measurements, FRET, FRAP, optogenetics and behavioral tests in rodents.

Member/s of the lab who will act as tutor/co-tutor of the project (if different from the group IP):

Contact: Félix Viana/Jorge Fernández Trillo