

**Group name: Sensory Transduction and Nociception Group**

**IP name: Ana Gomis**

**Group web: <http://painchannels.com/index.php/index>**

**Title of the MRP/TFM:**

**Control of mechanosensitive Piezo channels by light**

Summary of the Project:

Mechanically-activated channels are membrane proteins that open in response to mechanical stimuli. PIEZO1 and PIEZO2 are two of the mayor cellular mechanotransducers, essential for basic cellular processes like the sense of touch, proprioception and bone development. However, their study has been hampered due to the lack of selective pharmacological tools.

Recently, the first opto-gated mechanosensitive channel was developed (mOP1) based on a tethered photoswitch, attached to a single engineered mutant near the pore region of the channel, allowing optical control over PIEZO1 channels.

Giving the importance of Piezo 2 channels on light touch, proprioception and inflammatory pain and the lack of pharmacological tools to modulate it, it is of special interest the development of an opto-gated PIEZO2. This could be achieved thanks to the huge similarity between PIEZO1 and PIEZO2 amino acid sequence in the pore region. The aim of the project is to test whether photoswitch labeling of PIEZO2 point mutations confers light sensitivity to the channel.

Specific aims:

To perform site directed mutagenesis on a PIEZO2 coding sequence containing plasmid.

To characterize light-gated ion currents on cells expressing PIEZO2 mutants labeled with a photoswitch.

Methods and technology involved in the MRP/TFM Project:

The student will learn to culture cell lines and to perform cDNA transfection, as well as molecular biology techniques as western blot and PCR and patch clamp recordings.

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: Ana Gomis/Francisco Peralta**