

**Name of grant holder: S.M. Géranton**

**Project title: FKBP51 and chronic pain states**

This is a report describing the activities related to the grant named above that have occurred during the first 6 months of the project.

**Project aims**

We have recently shown that blocking FKBP51, a protein important for the regulation of the stress response, could interrupt a pre-existing chronic pain states in mice. The aim of this project is to test the efficacy of a novel FKBP51 inhibitor, SAFit2, in clinically relevant models of pain states. In particular, we want to test the effects of FKBP51 inhibition in 3 rodent models: a surgical model of skin incision; a model of chemotherapy induced neuropathic pain and a model of diabetes induced pain. This project will also use a range of molecular techniques to further our understanding of the mechanisms involved.

**Progress so far**

This grant is well on track:

1. We have been able to demonstrate that FKBP51 inhibition using SAFit2 cannot improve the mechanical hypersensitivity that develops after a single incision of the skin in the plantar surface of the hindpaw. This was not surprising as we had found before that FKBP51 inhibition only improved longer-lasting pain states. These results help us further characterise the type of pain modulated by FKBP51.
2. We have developed a mouse model of chemotherapy (paclitaxel) induced pain and using this model we have preliminary data indicating that inhibition of FKBP51 with SAFit2 can improve the mechanical sensitivity that develops in this model. These experiments will be completed in the next 6 months of this project.
3. We have analysed the cell specificity of FKBP51 expression in the superficial dorsal horn and found that FKBP51 was expressed in both neurones and astrocytes but at different levels.

**Data dissemination**

Part of the data has been discussed at a meeting: Talent Innovation Pain; La Spezia, Italy. Oral presentation given by Dr. Maria Maiarù, 20<sup>th</sup> - 21<sup>st</sup> of April, 2017. We will continue and present the data at national and international meetings. The data will also complete data previously acquired to be part of a manuscript that we will publish in a high-impact scientific journal (manuscript already in preparation).

S.M. Géranton; FKBP51 and chronic pain states; grant report: first 6 months.