

## Locus Coeruleus-Pain (LOCUS COERULEUS-PAIN)

### Resumen:

People Programme in the FP7

### Objetivos:

The locus coeruleus, the main source of noradrenaline in the central nervous system, is a crucial step in both the descending and ascending pain modulatory systems which are compromised in neuropathic pain. Neuropathic pain is a chronic pathological condition arising from damage in the nervous system and that does not respond successfully to conventional analgesics. In fact, the first-line treatment approaches for neuropathic pain belong to drugs that modulate the activity of the locus coeruleus. In spite of this, LC role in neuropathic pain remains unknown. Locus coeruleus neuronal activity is modulated, among others, by G-protein-coupled receptors,  $\alpha_2$ -adrenoceptors presynaptically located. Indeed, the activation of these autoreceptors by noradrenaline circulating in the milieu active G protein-activated inwardly rectifying K<sup>+</sup> channels (GIRK), hyperpolarizing the cell and inhibiting the release of the own neurotransmitter at LC level and projecting areas such as the spinal cord. This is a physiological feedback mechanism that control noradrenaline extracellular levels and consequently pain threshold. Thus,  $\alpha_2$ -adrenoceptors and GIRK channels seems to be a significant player in the locus coeruleus action potential frequency and therefore in the noradrenaline synaptic concentration. Thus, we suggest that they will play an essential role in ascending and descending pain transmission involved in neuropathic pain and that the knowledge of physiological processes responsible for their contribution to pain threshold will help to the design of a new line of anti-neuropathic drugs. We will tackle the project by implementing a broad range of techniques, from single-cell electrophysiology to whole-animal behavioural studies, and by correlating the results obtained by different techniques throughout the project.

### Objetivos contribución:

The University of Cadiz is the only participant of this Project, so the contribution is 100%.

### Impacto:

- 1) To develop new drugs based on rational design from the pathophysiological knowledge.
- 2) The data and findings of research proposals, and the results of the previous project FIS are and will be disseminated to the scientific community and society at large through the website: <http://antidepressivosydolor.areastematicas.com/> Spanish Society of Pain.
- 3) This project seeks to answer a question raised both preclinical level but above all clinical. We hope that the combination of different experimental approaches we raised lead to publications in journals of wide circulation and quality.

**Presupuesto:** 45,000.00

### Equipo de investigación

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**Presupuesto del equipo:** 45,000.00

**Universidad:** Universidad de Cádiz

**Estado:** published

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