

ESR 9

THE PROJECT: Sexual dimorphism in pain-depression interactions: a role for the endocannabinoid system?

Objectives

To determine whether anxiodepressive phenotypes in rat models of neuropathic pain:

- 1/ Exhibit sexual dimorphism, and the extent to which this is associated with alterations in the spinal and supraspinal endocannabinoid system
- 2/ Are sensitive to pharmacological manipulation of the endocannabinoid system, and determine the brain regions involved
- 3/ Are sensitive to deep brain stimulation (DBS), and the extent to which the effects of DBS may be mediated by alterations in the endocannabinoid system.

Methodology

Rat models of neuropathic pain and tests of relevance to anxiety and depression (e.g. open field, elevated plus maze, forced swim test, sucrose preference). Rats of both sexes will be used. RT-qPCR, Western blotting, RNA scope and/or immunohistochemistry for analysis of cannabinoid receptor expression, and HPLC with mass spectrometry for measurement of amygdalar endocannabinoid levels. Assessment of microtubule dynamics by Western blotting and immunohistochemistry. Targeted pharmacological studies will determine the effects of manipulating the endocannabinoid system. Deep brain stimulation (DBS) within key brain regions implicated in endocannabinoid-mediated regulation of sexual dimorphism.

Expected Results

This project will provide novel data on sexual dimorphism and pain-related negative affect, and the involvement of the endocannabinoid system. Novel data on the effects of DBS on pain-related negative affect in a sex-dependent manner, and involvement of the endocannabinoid system. Training in integrative neuroscience. The recruited researcher will be trained in and use state-of-the-art methodologies, learn about neurobiology of neuropathic pain, the psychobiology of affective processes, the endocannabinoid system, brain pathways, and examine novel treatment strategies for chronic neuropathic pain (e.g. DBS, endocannabinoid system modulators).

Supervisors and host organisations

Main supervisors and recruiting organisation:

David Finn and Michelle Roche

Pharmacology and Therapeutics, Physiology, School of Medicine, National University of Ireland Galway

Co-supervisor (academic partner):

Esther Berrocoso,
University of Cadiz,
Spain

Co-supervisor (non-academic partner):

Transpharmation Ireland (Jack Prenderville and Ewa Sokolowska), based in Dublin or Galway

Planned mobility track and secondments:

NUI Galway, Ireland: M1-16, M32-36: Behavioural studies and endocannabinoid system analysis using molecular and neurochemical methodologies.

University of Cadiz, Spain: M17-28: Training in deep brain stimulation (DBS).

Transpharmation Ireland: M29-31: Assessment of markers of synaptic plasticity; ESR to be located in Dublin or Galway

Enrolment in Doctoral degrees:

National University of Ireland Galway and University of Cadiz/ Joint Diploma

THE POSITION

Duration

36 months

Salary

Living allowance €3780 per month (gross)

Allowance

Mobility allowance €600 per month. Family allowance €250 per month.

THE CANDIDATE PROFILE

Academic prerequisite

Candidates must hold a first class or upper second class honors BSc in a relevant biology-based subject (physiology, pharmacology, neuroscience, anatomy, biochemistry, biomedical science, or equivalent). A relevant MSc degree and/or significant research experience (>6months) would be an advantage.

Knowledge on specific topics

Applicants must demonstrate a keen interest in pre-clinical research in the area of neuroscience and the endocannabinoid system relating to affective disorders and pain

Technical skills

Experience in at least two of the following is desirable: Behavioural neuroscience; pre-clinical (rodent) models of pain, stress, anxiety, depression; stereotaxic/small animal surgery; intracerebral microinjection; *in vivo* electrophysiology; immunohistochemistry/immunocytochemistry; RNAscope; FACS analysis of inflammatory cells/mediators; Western immunoblotting; ELISA; RT-qPCR; radioligand binding ; HPLC ; Mass Spectrometry.

Exclusion criteria

Researchers can be of **any nationality**. However, the candidate **must not have resided** or carried out their main activity (work, studies, etc.) **in Ireland** for more than 12 months in the 3 years immediately before the recruitment date. Compulsory national service, short stays such as holidays, and time spent as part of a procedure for obtaining refugee status under the Geneva Convention¹ are not taken into account.

The candidate shall, at the time of recruitment, be in the **first four years** (full-time equivalent research experience) of their research career and **have not been awarded a doctoral degree**.

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before the 1st August 2021**