Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2024-2025

Project Nº 43

Title: Brain-immune system interactions in major depression:role of HDAC5 in prefrontal cortex neurons and myeloid cells

Department/ Laboratory *Laboratory of Pharmacology, Department of Pharmaceutical Sciences, University of Navarra*

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The epigenetic hypothesis of depression suggests, essentially, that depression is linked to failure in synaptic plasticity in limbic brain regions in which epigenetic mechanism could play a key role. Among them, histone posttranslational modifications such as histone deacetylation by specific histone deacetylases (HDACs) could trigger neuronal plasticity failure. In the CNS, multiple HDACs could impair neuronal repairing processes. We have recently carried out a study focused on the regulation of different HDACs and other associated genes in monocytes and T-cells of depressed patients (project supported by Health department of Navarra´s Government, call 2017-2021). Within this project, 56 patients with severe-moderate MD were recruited together with age-sex matched healthy volunteers. The severity of the illness was assessed using the MADRS (Montgomery-Asberg) scale. In this study altered expression of three biomarkers (HDAC5, BDNF, β2 adrenoceptors) were found in immune cells suggesting that they could form part of the immune clinical scenario of MD. Importantly, these changes had been previously observed in post-mortem brain of MD patients as well as in the PFC of mice exposed to depression models. Thus, brain-immune interactions in the modulation of these biomarkers might exist in MD. The aim of this project (objective 1) is to explore whether the alterations observed also occur in hematopoietic progenitor cells. If this is the case, it could be suggested that MD is linked to stable epigenetic alterations in the cells that precede to other biological or environmental risk factors.
Specifically, (objective 1) we will study the influence of MD in the expression and cellular localization of HDAC5 and BDNF expression in CD34+, classic monocytes and T-cells from peripheral blood of depressed patients. Secondly, (objective 2) we aim to study the effect of HDAC5 overexpression in the brain and in myeloid cells of mice on BDNF expression and depressive-like behavior

yes	x
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator? Depending on the motivation of the Master student, one objective (objective 2) of the project will include animal manipulation.

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