

## **Research Project Proposal**

Academic year 2020-2021

## Máster en Investigación Biomédica

## Project Nº 49

Title: Identificantion of candidate genes conferring resistance to dementia in the context of Alzheimer's Disease

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## Summary

Clinical studies revealed that some aged-individuals accumulate a significant number of histopathological Alzheimer's disease (AD) lesions in their brain, yet without developing any signs of dementia. In this context, animal models of AD represent suitable tools to identify genes that might promote cognitive resilience. In a recent study of our lab cognitively resilient individuals (close to 20%) in the aged-Tg2576 mouse model have been identified. A transcriptomic analysis of these mice identified several **genes that might confer resistance to dementia**. The overall goal of this project is to **elucidate the role of some of these genes in the pathophysiology of AD**. First, to determine weather changes in the expression levels of these genes could be underlying the discordance between AD pathology and dementia, human brain samples from early and late stages of AD patients and healthy individuals will be employed. Likewise, a different mouse model (APP/PS1) will be employed to analyze the role of select genes in memory function. Basal gene expression levels will be analyzed at different time-points (with and early and late –phenotype) and also when the animals are subjected to different memory tasks such as the Fear Conditioning or the Morris water maze test. In parallel, primary neuronal culture of these mice will be employed to analyze cellular responses to overexpression or knockdown of candidate genes.

\* Different biochemical techniques such as real-time- PCR, western-blot analysis or immunohistochemistry will be employed in the project.

yes X no Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?