Project Nº 38
Title: IL-1β receptor inhibition as a new therapeutic approach for Alzheimer's disease

Department/ Laboratory
Therapeutic Genes for Neurodegenerative disease´s lab (Lab. 2.06)
Division of Gene Therapy for Neurological Disorders - CIMA

Director 1 *Mar Cuadrado Tejedor*
Contact: *mcuadrado@unav.es*
Codirector: Ana García Osta
Contact: *agosta@unav.es*

Summary

Inflammation is one of the main features of Alzheimer's disease (AD), however, its impact on disease progression and neurodegeneration is not completely elucidated. Among the different cytokines associated with AD, IL-1b seems to play a pathogenic role. Accordingly, we have recently demonstrated that blockade of the IL-1 receptor with anakinra resulted in a significant increase in cognitive capacity not only in healthy mice, but also in the APP/PS1 AD model. Interestingly, the analysis of the brains of these APP/PS1 treated mice showed an important attenuation of tau pathology as well as a reduction of the inflammatory response. Considering these positive results, in the present project, in order to reduce systemic exposure and possible side effects of a chronic systemic administration, we aim to test this therapeutic approach by using an intranasal administration based on a hydrogel containing IL-1βR inhibitor-based nanoparticles. For this purpose, to compare both routes of administration APP/PS1 and WT mice of 6-8 month-old will be treated intraperitoneal or intranasally (n=8-10) and two months later will phenotypically characterized. To test memory function, several behavioral paradigms (object recognition, fear conditioning or the Morris water maze test) will be used and to analyze the pathological signs of the AD brains, different biochemical techniques such as real time PCR, western-blot or immunohistochemistry will be used.

yes	X
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?