Project Nº 24
Title: *"Overexpression of mutated tau in the brain of APP/PS1 mice using adenoassociated virus (AAV) as a preclinical model of Alzheimer´s disease"*

Department/ Laboratory *Neurobiology of Alzheimer´s disease Lab.2.06 CIMA*

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Summary

Alzheimer´s disease (AD) which is the most common form of dementia in the elderly is pathologically characterized by the presence in the brain of extracellular plaques comprised of aggregated amylod-β peptide and intracellular neurofibrillary tangles that mainly contain the hyperphosphorylated tau protein. These hallmarks provoke a neuronal dysfunction that ultimately leads to the neuronal loss observed in the atrophic brain of AD patients.

Over the last decade, our research group has used amyloid-transgenic mice (Tg2576 and APP/PS1) as preclinical models of AD. So far these models do not recapitulate certain neuropathological signs, such as tau aggregation (neurofibrillary tangles) and/or neuronal loss that are presented in the human condition.

Taking into account that animal models are indeed mandatory for preclinical studies and that different therapeutic approaches are planned to be tested in the lab, in the present project we consider by using AAVs, to generate a new tool which more reliably mimic the AD-related pathology.

Accordingly, to generate such a model, we plan to virally induce the expression of P301L human Tau, which is the most prevailing mutation in various types of 4R tauopathies, in different brain regions of the APP/PS1 mouse by stereotactic injection. At different time-points, animals will be functionally and biochemically characterized: to test memory function, behavioural paradigms (object recognition, fear conditioning or the Morris water maze test) will be used, while to analyze pathological signs of the AD brains, different biochemical techniques such as real-time- PCR, western-blot analysis or immunohistochemistry will be used.

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