



Research Project Proposal

Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 22		
Title: <i>Effect of Sirtuin2 inhibition in a transgenic mouse model of Alzheimer disease</i>		
Department/ Laboratory <i>Department de Pharmacology and Toxicology. University of Navarra.</i>		
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Summary <i>Short summary of the project with a maximum extension of 250 words, including the goals and the methodology that will be used.</i> <i>Epigenetic changes are currently recognized as part of the aging process and have been involved in many age-related diseases, including Alzheimer Disease (AD). Sirtuins, which are nicotinamide adenine dinucleotide (NAD)⁺-dependent class III histone deacetylases, have emerged as master regulators of metabolism and longevity. Among all sirtuins, Sirtuin 2 (SIRT2) is the most expressed in the central nervous system (CNS) and has been involved in a variety of biological processes however, its specific functions remain unknown.</i> <i>It has been described an age-dependent accumulation of SIRT2 in the brain. Interestingly, while sirtuin 2 (SIRT2) increased CNS levels have been linked to aging, SIRT2 inhibition could be a novel therapeutic strategy for neurodegenerative diseases. To test this hypothesis the APP/PS1 mouse model, which resembles the main neuropathological hallmarks of AD, will be used. The SIRT2-selective inhibitor, compound 33i, will be administered everyday i.p to 6 month old APP/PS1 and wild type for two months. Then, the cognitive function will be evaluated by the Morris Water Maze and the Novel object recognition test. After sacrifice, the neuropathological hallmarks of AD (Tau pathology, β-amyloid, neuroinflammation, synaptic dysfunction and autophagy) will be analyzed via western-blot, qPCR and immunohistochemistry. If the combined results of this study decipher the implication of SIRT2 in these mechanisms, the present project would provide an ideal novel target to treat age-related cognitive deficits, AD and other neurodegenerative diseases.</i>		
yes	<input checked="" type="checkbox"/>	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	<input type="checkbox"/>	