MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2022-2023

Project Nº 06

Title: *Deciphering the role of astrocytic GLUT1 in Alzheimer's disease*

Department/ Laboratory
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Summary
Cerebral blood vessels are sheathed by endothelial cells that interact with astrocytes, regulating the entry of nutrients, such as glucose. Regulation of blood glucose supply to the brain is controlled via GLUT1. GLUT1 is highly expressed in both endothelial cells and astrocytes, but it is more abundant in astrocytes. Thus, astrocytes are located at the interface between vessels and neurons, putting them in a privileged position to control brain glucose uptake.

Preclinical period of Alzheimer's disease (AD) is characterized by diminished glucose consumption. However, it is not known what the contribution of glial cells in this low glucose uptake is. To uncover this, we will use a tamoxifen-inducible Cre/loxP approach to genetically remove GLUT1 exclusively from astrocytes in a time-specific fashion. To assess if GLUT1 deletion impacts in the progression of AD these mice will be crossed with the APP/PS1 model. Also, if a treatment with VEGF can restore glucose uptake will be assessed.

The overarching aim of the present project is to assess if GLUT1 reductions in astrocytes can lead to cerebrovascular damage contributing to and/or accelerating AD-like neurodegeneration. To this end, the specific aims of the project are:

- To assess the impact of GLUT1 astrocytic ablation on glucose uptake and glucose sensing in the brain.
- To check microvascular alteration, cerebral blood flow and blood brain barrier (BBB) breakdown after GLUT1 astrocytic ablation.
- To study cognitive consequences of GLUT1 astrocytic ablation on AD mice.
- To analyze if astrocytic GLUT1 deficiency accelerates cerebral β-amyloidosis.

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yes	x
no	

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