Research Project Proposal
Academic year 2020-2021
Máster en Investigación Biomédica

Project Nº 03
Title: *Impact of astrocytic insulin receptor on glucose uptake and cognition*
Department/ Laboratory *Department of Pharmacology and Toxicology, School of Pharmacy and Nutrition*
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Summary

Brain insulin signaling has faced a new and increasing interest in neuroscience research because of its multifaceted and spatially compartmentalized actions. Within those actions on the brain, insulin may also modulate neurobehavioral processes, including cognition. While most of these effects are thought to occur through insulin action on neurons, recently it has been shown that insulin may also act on astrocytes.

The present study, aims to investigate the role of astrocytic IR in both bioenergetic coupling and neurobehavioral performance. Therefore, the overarching aim of the present project is to assess if IR reductions in astrocytes can induce changes in glucose uptake and induce brain alterations.

To uncover this aim *C. elegans* as experimental model will be used. The nervous system of *C. elegans* consists of 302 neurons and 56 glial cells. Within the 56 glial cells, the CEPsh glia are considered the equivalent to the mammal astrocytes in the worm. To enable conditional protein depletion in *C. elegans* we will use auxin-inducible degradation (AID) system. To remove IR specifically in CEPsh glia, the endogenous locus of daf-2 (IR gene in the worm) will be tagged with the degron sequence and this worm will be crossed with another which expresses TIR1 under the hlh-17 promoter (specific of CEPsh glia).

In this experimental model we will perform the following specific aims:

1. Assess the impact of Daf-2 ablation on glucose availability
2. Assess the impact of Daf-2 ablation on ATP release
3. **Study behavioral consequences of astrocytic Daf-2 ablation**

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