



MASTER'S DEGREE IN BIOMEDICAL RESEARCH

Research Project Proposal

Academic year 2024-2025

Project Nº 14

Title: Impact of astrocytic insulin receptor ablation on astrocytic calcium dynamics

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Summary Short summary of the project with a maximum extension of 250 words, including the goals and the methodology that will be used

The ever-increasing life expectancy, with a sedentary lifestyle and altered eating habits, has led to an increase in the prevalence of age-related diseases such as type 2 diabetes (T2DM) and Alzheimer's disease (AD). Converging evidence has indicated that insulin resistance in the central nervous system is observed in both T2DM and AD, leading to the hypothesis that impaired neuronal insulin action might be a unifying mechanism in the development of both diseases. This assumption, however, is in contrast to the protective role of impaired insulin signaling in aging and in diseases such as AD.

Mice lacking insulin receptor (IR) in neurons display metabolic abnormalities; however, the role of insulin action on astrocytes remains less studied. To uncover the role of astrocytic IR, tamoxifen-inducible Cre/loxP approach will be used achieve time-specific IR deletion exclusively in astrocytes.

The overarching aim of the present project is to assess if IR reductions in astrocytes can induce cognitive deficiencies and to study if those cognitive changes are linked to changes y astrocytic calcium dynamis.

The specific aims of the project are:

- To study cognitive consequences of IR astrocytic ablation.

The effects on cognition will be evaluated using behavioural tests such as morris water maze and fear conditioning.

- To assess the impact of astrocytic IR ablation on Ca2+ dynamics

To this end the technology of fiber photometry will be employed in awake mice while doing a behavioral task.

- To test if Ca2+ changes can rescue cognitive deficiencies.

Astrocytic Ca2+ dynamics modification will be induced by DREADDs technology.

yes	X
no	

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