Research Project Proposal
Academic year 2019-2020

Project Nº 17	
Title: *Impact of astrocytic insulin receptor on cognition*	
Department/ Laboratory *Department of Pharmacology and Toxicology, School of Pharmacy and Nutrition*	
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Summary

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. The specific aims of the project are:

- To assess the impact of IR astrocytic ablation on glucose uptake and glucose sensing in the brain.
  This would be studied by FDG-PET and cells glycolytic rate and mitochondrial respiration.
- To check microvascular alteration, cerebral blood flow and blood brain barrier (BBB) breakdown after IR astrocytic ablation.
  Astrocytic end-feets are essential for the BBB structure, therefore IR ablation in these cells could have an impact in the BBB stabilization.
- To study cognitive consequences of IR astrocytic ablation.
  The effects on cognition will be evaluated using behavioural tests such as morris water maze and novel object recognition tes

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