Datum: 2025-10-06
Diarienr: GU 2025/3543

Training Plan

Background

Neonatal brain injury remains a global health burden, main factors include prematurity, hypoxia-ischemia (HI) and infection. There are currently limited available therapies, with hypothermia being only administered in term HI infants. However, up to 50% of treated neonates still develop neurological impairments. Using the mouse HI model we have established that exendin-4, a GLP-1R agonist used for the treatment of type-2 diabetes mellitus, is significantly neuroprotective. Additionally, a single dose of exendin-4 enhanced hypothermia protective effect.

Purpose

The project aims to understand how exendin-4 confers neuroprotection against neonatal brain injury. The aim of this project is to generate further data that may support the use of exendin-4 for future interventions in neonatal brain injury in the clinic.

Method and Work Plan/Schedule

We will work with animal tissue brain samples that have had hypoxia-ischemia and/or infection. A subset of these groups will have received exendin-4 as a treatment. The different brain tissue samples will be processed to further characterize these injury models in animals and better identify the mechanisms of injury. This will be achieved by looking at markers of injury, such as TUNEL, caspase-3, MAP-2- and MBP-positive tissue loss. These results will help to understand how exendin-4 may confer neuroprotection by investigating its effect in different affected brain regions and structures and look at its protective effects across different neural cells, including neurons, astroglia, microglia and oligodendrocytes. This will be achieved by looking at cell survival, as well as morphological changes. Additionally, mitochondrial function and cytokine release will be analyzed and compared between treated and untreated groups, as exendin-4 has been shown to have strong mitoprotective and anti-inflammatory properties.

Learning outcome

During the project the student will learn techniques related to histology, including tissue paraffin embedding, microtome sectioning, histology, immunohistochemistry and immunofluorescence. The student will also learn different microscopy techniques, such as cell counting, threshold luminosity, convex hull area and soma cell area. Additionally, the student will also learn how to perform ELISA assays and will be introduced to Seahorse technique.

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Scholar (printed name)	Supervisor (printed name)

A copy of this plan is to be handed to the scholar after his/her signature.