



Research Project Proposal
Academic year 2019-2020

Project Nº 12

Title: *Optimization of gene transfer strategies for brain diseases.*

Department/ Laboratory *Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc.*

Gene therapy and regulation of gene expression program. CIMA.

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Summary

The efficient transfer of large fragments of DNA into the brain is an unmet scientific and medical need. Many monogenic diseases affecting brain functions are caused by defects in genes that exceed the cloning capacity of conventional gene therapy vectors.

We propose the development of High-Capacity Adenoviral vectors (HC-Ad), which can deliver DNA sequences up to 36 Kb in length, and maintain expression for several years after a single vector administration.

In this line of research we will evaluate different routes of administration (intra-parenchymal, intra-ventricular and intra-arterial), in combination with different strategies to achieve transient disruption of the blood brain barrier and/or the ependymal barrier. The student's project will contribute to the advance of these tasks at different stages.

In addition, we will implement modifications in the vector capsid and the expression cassettes in order to target transduction and gene expression in specific neuronal populations.

Evaluation of the new vectors will be performed in cell cultures and in mice. We will employ reporter genes (Luciferase/GFP) for analysis of intensity and location of transgene expression.

The project involves a wide variety of techniques including molecular biology (construction of plasmids), cell biology (cell culture and transfections), immunohistochemistry and supervised animal experimentation in mice (evaluation of transgene expression in vivo).

yes	<input checked="" type="checkbox"/>	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	<input type="checkbox"/>	

yes	<input checked="" type="checkbox"/>
no	<input type="checkbox"/>