Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2022-2023

Project Nº 11

Title: *Development of DNA trans-complementation strategies for expression of large genes in the brain.*

Department/ Laboratory *Gene Therapy and Regulation of Gene Expression Program. CIMA.*

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Summary

Vectors derived from Adeno-Associated Virus (AAV) are widely used in gene therapy clinical trials for the treatment of a variety of diseases. New AAV variants obtained by capsid engineering provide unique opportunities for gene transfer into the brain. However, the cloning capacity of AAV vectors is relatively low (4.7 Kb). Therefore, single AAV vectors are not suitable for a large number of human diseases.
The aim of this project is to apply techniques of DNA trans-complementation to increase the scope of AAV vectors in the brain.
We will employ GFP as a reporter gene, and new AAV vectors capable to cross the blood brain barrier. The GFP coding sequence will be split in two fragments, fused with recombinogenic sequences. Transfection of AAV genomes in cell cultures will be employed to evaluate the ability to restore the full sequence and to express the intact GFP protein. The optimal conformations will used to generate a pair of AAV vectors, and they will be evaluated in mice following different routes of administration. The efficacy of transduction and the identity of GFP+ cells will be studied by immunofluorescence.
We hope to generate new tools for further development of gene therapy strategies against genetic encephalopathies.

yes	X
no	

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