Universidad de Navarra
Facultad de Ciencias

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

Project Nº 32

Title: Development of novel AAV vectors for the treatment of Cx26 deficiency

Department/ Laboratory *Gene Therapy for Hepatic disorders lab / Gene Therapy and Regulation of Gene Expression department (CIMA)*

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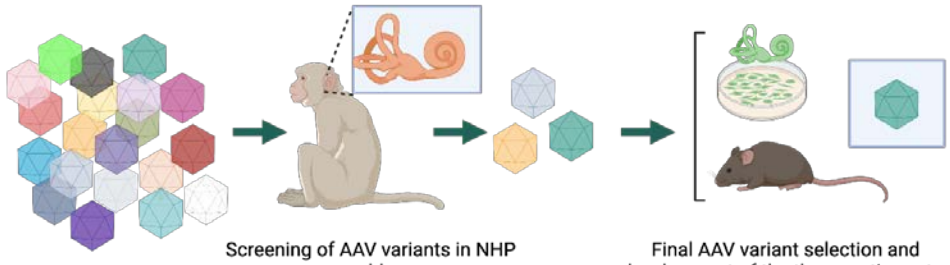
Summary

Hearing loss is the most common sensory impairment in the population, with more than 400 million affected worldwide. More than half the cases of non-syndromic profound congenital hearing loss have a genetic cause, and most (~80%) are autosomal recessive, with a prevalence of about 1-2 every 1000 births. The most common genetic cause of hearing loss is caused by a loss of function mutation in the *GJB2* gene which encodes for Connexin 26 (Cx26), a gap junction protein highly expressed in vestibular organs, but also by the supporting cells in the cochlea. The curative treatment for Cx26 deficiency requires the restoration of Cx26 expression to appropriate levels in the affected cells of the cochlea. To achieve this goal the aim of the project is to develop and validate a personalized gene therapy for Cx26 deficiency. The strategy is focused on 1) Selecting the most efficient AAV capsids targeting the cochlea in the relevant preclinical NHP model, which will enable the most effective preclinical evaluation and validation of novel gene therapeutics before clinical evaluation in human patients, and 2) Development of the therapeutic vector for Cx26 deficiency (Figure 1).



Screening of AAV variants in NHP cochlea

Final AAV variant selection and development of the therapeutic vector for Cx26 deficiency in the *Gjb2* KO mouse model and human cochlear explants.

The team is currently working on the capsid selection in NHP so the Master project will be focused on the optimization of NHP sample processing for single cell sequencing and bioinformatic analysis with the goal of selecting 3 to 5 relevant AAV variants targeting *GJB2* expressing cells and regulatory elements (promoter, enhancer, others) highly expressed in those cells. With that information we will start the generation of a highly specific therapeutic expression cassette encoding the *GJB2* gene.

yes	X
no	

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