Universidad de Navarra
Facultad de Ciencias

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2023-2024

Project Nº 51

Title: Development of novel AAV vectors for precision gene medicine of congenital hearing loss

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

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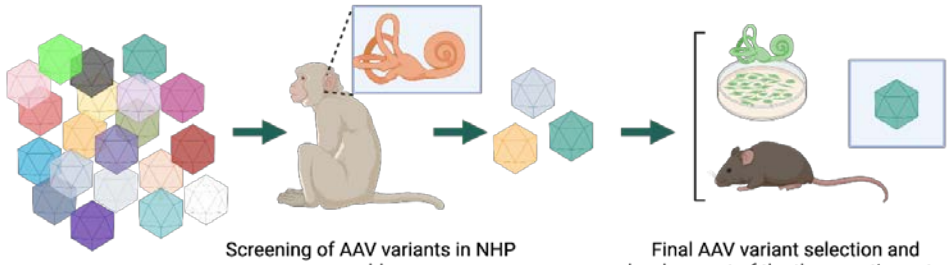
Summary

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 do so our lab has already performed an AAV capsid screening in non-human primates (NHP) to select the most efficient AAV variants targeting the cochlea as well as cell-specific regulatory elements based on RNA sequencing data (Figure 1, step 1). The team is currently working on the generation of the therapeutic expression cassette based on the data generated in step 1. **The Master project will be focused on the validation of 3 to 5 relevant AAV variants *in vitro* and *in vivo* as well as the characterization of the GJB2 therapeutic vector in the Gjb2 KO mouse model.** (Figure 1, step 2). Methodology includes cloning, cell culture, QPCR, protein detection by immunofluorescence and western blot, animal handing and animal sample processing.



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.

yes	X
no	

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