Universidad de Navarra

Research Project Proposal
Academic year 2024-2025

Project Nº 06

Title: *Development of chimeric AAVs for Tissue Targeting*

Department/ Laboratory *Lab 4.04. Gene Therapy and Regulation of Gene Expression. CIMA*

Director 1 *Rafael Aldabe Arregui*
Contact: *raldabe@unav.es*

Summary

The project presented herein is a key component of our recently established "Genetic Drones" platform, which aims to revolutionize gene therapy vector technology by coating viral vectors with nanomaterials and various molecules such as glycans and aptamers and/or generating AAV genetic variants. This novel approach allows for the modification of vector properties enhancing their specificity and enabling targeted delivery to specific cell types.

Our primary focus is on the kidney, a complex organ afflicted by numerous genetic diseases, including the highly prevalent autosomal dominant polycystic kidney disease (ADPKD). Currently, there are no existing vectors capable of efficiently delivering therapeutic genes to renal cells. Thus, our main objective is to develop the first gene therapy vectors specifically designed for the treatment of kidney diseases. To accomplish this, we have established a series of intermediate objectives:

1. Construction of chimeric vectors based on adeno-associated viruses (AAVs), incorporating glycans and/or aptamers on their surface or modifying genetically their capsid.
2. Evaluation of the infectivity and performance of these chimeric vectors in both cell culture and in vivo models.
3. Selection of chimeric vectors with optimal renal transduction profiles following local administration.

To achieve these objectives, we will employ a range of methodologies including molecular biology techniques, cell culture experiments, production, purification, and modification of recombinant AAV viruses with nanomaterials. The generated viruses will undergo extensive characterization through PCR, western blot analysis, structural studies, and infectivity assays. Furthermore, we will conduct renal inoculation of the developed vectors and perform comprehensive biochemical, histological, and molecular analyses on treated animals.

yes	X
no	

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