Research Project Proposal
Academic year 2018-2019

Project Nº 14

Title: *Improvement of gene therapy vectors for treatment of metabolic rare diseases*

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

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Summary

Several clinical and preclinical studies have shown gene therapy based on the AAV viral vector is a real treatment option for monogenic metabolic diseases. However there is a limitation for an effective early treatment: when gene therapy vectors transduce immature livers there is a progressive elimination of the vector molecules limiting treatment efficacy. In addition these treatments cannot be developed to target any diseased organ as they are based on the AAV natural tropism excluding organs with a high incidence of genetic diseases like kidneys.

We want to improve gene therapy vector tropism and potency when it is inoculated in neonatal liver and young kidneys. We are going to modify AAV viral genome with DNA sequences that will provide replication potential when cellular DNA is replicated, including maintenance in daughter cells when host organ grows, main limitation treating neonate/infant individuals. Moreover, we want to design vector tropism engineering vector capsid with moieties with a specific tropism (organ/cell type) that can transfer this targeting property to the vector. We will explore modifications that can provide renal tropism to AAVs in order to develop a gene therapy platform to treat renal diseases.

Therefore this project will include molecular biology techniques (PCR, DNA cloning, …), work with cells (transfection, virus production, cell infection, cell characterization [protein and gene expression by PCR, western blot, fluorescence microscopy]) and experiments with mice (virus inoculation, surgery, sacrifice, necropsy, …) analysing gene and protein expression in target organs (liver, kidney) using microdissection, microscopy and image analysis.

yes	**X**
no	

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