Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2017-2018
This form must be filled in ENGLISH

Project Nº 32
Title: **Gene correction for inborn errors of metabolism**
Department/ Laboratory Gene Therapy Program/Adenovirus vector lab. CIMA.
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Summary Inborn errors of metabolism can cause severe diseases with manifestations in infancy or later periods of life. The physiopathology of these diseases is usually associated with genetic defects affecting hepatic metabolism. Gene therapy approaches offer an etiological treatment for this group of diseases, especially taking into account the relatively high efficacy gene transfer achieved by vectors in the liver. However, regulation and long-term persistence of transgene expression are still big challenges. In contrast with the episomal supplementation of genes, gene editing offers the possibility of permanent restoration or compensation of the alterations responsible for genetic diseases. Selective integration of DNA is based on homologous recombination with the cellular genome. The efficacy of this process is increased by the induction of DNA double strand breaks in specific sequences. Nucleases based in the CRISPR/Cas9 system (clustered regularly interspaced short palindromic repeats) have boosted this field thanks to their versatility. However, the frequency of DNA cleavage is much higher than the efficacy of recombination, increasing the probability of side effects and decreasing the therapeutic potential of this approach. In this work we will explore new strategies to confer a selective advantage of gene-edited cells and to enhance homologous recombination, with the aim of increasing the clinical relevance of gene editing strategies. *Please note that accreditation for animal manipulation may be required to carry out this project.