Research Project Proposal
Academic year 2021-2022
Máster en Investigación Biomédica

Project Nº 32	
Title: Optimization of methods to produce High-Capacity Adenoviral vectors for gene therapy applications	
Department/ Laboratory Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc. Gene Therapy and Regulation of Gene Expression Program. CIMA.	
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Summary:

High-Capacity Adenoviral vectors (HC-AdV) enable efficient transfer of large DNA cargoes, up to 36 Kb. The lack of viral genes in their genomes allows the expression of transgenes for long periods of time *in vivo*. Production of these vectors requires special protocols designed to complement all viral functions in cell culture (packaging cells). This is usually achieved by co-infection with a Helper Virus (HV). Both HC-AdV and HV replicate their genomes in the packaging cells. The HV encodes all proteins required for replication and capsid formation, but encapsidation of its genome is prevented by cleavage of its packaging signal by a recombinase (Cre) expressed by the cells. One of the limitations of this system is the genetic instability caused by chronic Cre recombinase exposure in packaging cells.

The aim of this project is to set up a modified production method in which packaging cells are not exposed to the function of Cre recombinase during their routine maintenance and amplification. Our preliminary results indicate that the new protocol improves the performance of the cells. The tasks of the project will be divided in two steps:

1. Optimization of the amplification and purification of HC-AdVs using the new method.
2. Application of the method to produce a new HC-AdV carrying large segments of human genomic DNA.

The student will learn concepts and skills related to virology, cell culture and molecular biology (plasmid construction).

yes		Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	X	