Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2022-2023

Project Nº 08

Title: *Inducible expression for gene therapy*

Department/ Laboratory *Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc.*
CIMA 306 and 406. Aptamer technology and gene therapy

Director 1 *Beatriz Moreno*
Contact: *bmbruma@unav.es*
Codirector: *Puri Fortes*
Contact: *pfortes@unav.es*

Summary

Gene therapy is expected to transform the health system in the coming years. Before, it is compulsory to have a technology that sustains the level of the therapeutic gene within the therapeutic threshold. Preferably, therapeutic levels should be controlled by clinicians with a simple drug. Drug dose should be adjusted for each patient to reach the ideal expression of the therapeutic gene and, therefore, the best efficacy. This describes an inducible system. Several inducible systems have been developed with little translation to the clinic. We are working to fill this gap. Using systematic evolution of a universe of RNA molecules, we have identified an RNA sequence that interacts with a cellular complex which blocks gene expression. In the presence of a specific drug, the RNA changes its structure hiding the inhibitor-binding sequence, leading to gene expression. Therefore, expression is normally OFF and turns gradually ON with increasing doses of the drug. Now, we want to modify the system with a simple trick to make it normally ON and turning OFF in the presence of the drug. Experiments will require cloning, transfection into cultured cells, evaluation of gene expression by RT-qPCR and FACS analyses, insertion into endogenous cells with CRISPR systems and, if possible, evaluation in model animals. This switch from DRUG-OFF to DRUG-ON is required by biotech companies to apply this technology to the development of safer CAR-T cells. In this way our technology will have a fast translation into the clinical setting for anticancer therapy.

yes	x
no	

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