Universidad de Navarra
Facultad de Ciencias

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2023-2024

Project Nº 39

Title: Molecular ROUTER, a method to control the expression of therapeutic genes with common drugs

Department/ Laboratory
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Summary

Gene Therapy and Immunotherapy have experienced an exponential growth, with many innovative treatments reaching the clinic. This has paralleled the generation and expansion of many Pharmaceutical Companies with gene and cell therapy products in their pipelines. However, most systems fail to control the therapy once administered to the patient. This is relevant because while high expression of the therapeutic gene associates with severe toxicities, low expression can be insufficient to reach a therapeutic threshold. Consequently, gene regulation systems which allow tight control over transgene levels are highly desired.

We have developed a molecular ROUTER to control the expression of therapeutic genes with common drugs: the amount of therapeutic gene expressed in the patient depends on the dose of a given drug. This can be reduced upon a severe adverse event, or alternatively increased if poor efficacy is observed**.** ROUTER is simple and robust but it is just at the first level of development. To unleash ROUTER's full potential and offer a final product to Pharma companies, we need to: (i) transfer ROUTERs that modulate polyadenylation to locations in which RNA splicing is changed in response to a drug, (ii) compare the performance in cultured cells of splicing, polyadenylation or ROUTERs with dual control, (iii) test ROUTERs responding to one or two drugs in order to build complex genetic circuits and (iv) transfer this technology to gene therapy approaches and evaluate the functionality in mouse models.

Methodology: Cloning, cell culture, luciferase and fluorescence-based assays, In vivo: handling, luciferase assays, drug administration.

yes	X
no	

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