Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2025-2026

Project Nº 30

Title: *Genetic engineering of inducible CAR-T cells for solid tumor Immunotherapy.*

Department/ Laboratory
Lab 4.06/3.06. DNA and RNA Medicine Department. CIMA.

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Summary
The recent FDA approval of several CAR-T cell-based therapies for hematological malignancies, together with the outstanding results observed compared to conventional chemotherapies in treated patients, has demonstrated the potential that this type of immunotherapy holds.
Despite their undeniable success, CAR-T cell therapies for solid tumors are, however, considerably more challenging. This is due to the presence of additional barriers they must overcome including: an immunosuppressive tumor microenvironment, compact extracellular matrix or high tumor genetic heterogeneity among other factors. Furthermore, in many cases, the lack of tumor-specific antigens makes some CAR T cell therapies riskier, given that severe inflammatory responses can be unleashed upon antigen recognition in healthy tissues.
In this regard, we propose the use of RNA-based molecular switches to regulate the expression of an in-house designed CAR targeting a tumor-associated extracellular matrix protein in an inducible and dose-dependent manner. Our switches are small and can fit into any viral vector of interest. Additionally, our switches do not rely on the expression of proteins, which could be a potential source of immunogenicity and compromise CAR-T cell long-term therapeutic effects.
The goal of this project is to characterize the effect of some of such molecular switches in the expression of our CAR of interest together with their capacity to modulate CAR T-cell antitumoral activity.
Methodology used: Flow cytometry, Lentiviral production and cell infection, ELISA, cellular assays (coculture, proliferation, cytotoxicity), isolation of human immune populations from healthy donors' peripheral blood samples, and molecular biology (cloning, PCR, DNA and RNA purification)

yes	
no	X

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