Universidad de Navarra

Facultad de Ciencias

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

Project Nº 10

Title: Innovative strategies to enhance CAR-T therapy through Adaptation to the tumor microenvironment

Department/ Laboratory
Immunology and Immunotherapy program.
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Summary

Despite the great success of chimeric antigen receptor (CAR) T cells as adoptive cell therapies in hematological tumors, poorer responses are being obtained in solid tumors. The tumor microenvironment (TME) interferes with T cell activity hindering T cell infiltration and promoting immunosuppression, exhaustion and limited persistence of CAR-T cells in vivo after their infusion. This limitation is partly attributed to the manufacturing process, during which T lymphocytes tend to acquire a terminal effector phenotype.

Hypothesis: Recent studies have shown that the initial hours following lymphocyte activation determine a metabolic and transcriptomic imprint that adapts to the conditions and nutrients available at the time of activation. This imprint involves epigenetic changes that are difficult to modify later, even if conditions and nutrient availability change. Based on this finding, we have formulated the hypothesis for this project: If we can induce CAR-T cell activation in an environment that more closely resembles the tumor microenvironment, we may be able to program their metabolism and function to be more permissive and effective in fighting the tumor. Our project is based on previous results on these innovative concepts to solve current drawbacks of CART cells in solid tumors.

The objective can be achieved by different methods, such as in vitro cell culture experiments including DNA and viral vector production, cell transduction, analysis of T cells effector functions (flow cytometry, ELISA, ELISPOT, cytotoxicity). Moreover, these therapies will be tested in in vivo experiments by using immunocompetent tumor models.

yes	x
no	

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