Universidad de Navarra
Facultad de Ciencias

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

Project Nº 27 ASIGNADO

Title: Improved CART cell design to overcome physical, chemical and cellular barriers found in the tumor microenvironment.

Department/ Laboratory
Immunology and Immunotherapy program.
Lab 3.02. CIMA.

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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 and exhaustion of CART cells. In fact, solid cancers have some formidable (i) physical, (ii) chemical and (iii) cellular barriers to the action of antitumor T lymphocytes and there is a clear unmet need for disruptive innovations to surpass these big challenges. In this project, we will work on three key challenges to improve the antitumor efficacy of CART cells in the hostile TME by: (i) targeting a key specific antigen presented in the tumor extracellular matrix and tumor neo-endothelium; (ii) Improving the adaptability and competitiveness of CARTs by equipping them with specific membrane transporters (amino acids/nutrients/ions transporters and exchangers) to adapt to the nutrient-deprived and acidic TME and; (III) combining CAR-T cell therapies with T regulatory cell inhibitors to improve their antitumor efficacy. 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?