Universidad de Navarra
Facultad de Ciencias

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2024-2025

Project Nº 33

Title: Targeting the myeloid compartment to improve immunotherapy of hepatocelular carcinoma

Department/ Laboratory
Laboratory 3.01. Program of Immunology and Immunotherapy, CIMA.

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Summary *Short summary of the project with a **maximum extension of 250 words**, including the goals and the methodology that will be used*

Immune checkpoint inhibitor (ICI)-based immunotherapy in hepatocellular carcinoma (HCC) promotes clinical responses in 30% of patients, mainly those with an enriched lymphocytic infiltrate. By contrast, patients with immunosuppressive myeloid cells have poorer responses. Macrophages and other myeloid cells shape the tumor microenvironment (TME) and modulate antitumor T cell immunity. Therefore, the **goal** of this project is to determine the therapeutic efficacy of combinations of ICI plus immunomodulators of myeloid cells. **Methodology** will include analysis by multiparametric flow cytometry of TME in different murine models, to select those more representative of myeloid enriched tumors. Relevant myeloid targets will be identified by analysis of human and murine HCC public databases. Selected models will be used in experiments of immunotherapy, where the efficacy of combinations of ICI plus myeloid cell-targeting agents will be tested. This will be accompanied by analysis of immune-associated mechanisms by flow cytometry, including lymphocytes and myeloid cells. Moreover, functional assays of T cell activation (ELISPOT, ELISA) upon antigen stimulation will determine T cell fitness. Finally, gene expression analyses by RNA-seq and RT-PCR, as well as immunohistochemistry, will be used to have an overall picture of the TME changes induced upon treatment.

yes	x
no	

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