Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2022-2023

Project Nº 41

Title: Novel cellular strategies to improve immunotherapy: targeting amino acid transporters on T cells

Department/ Laboratory
Juan Jose Lasarte's Laboratory (Lab 3.02), Immunology and Immunotherapy Department, CIMA.

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Glutamine (Gln) is an immunomodulatory amino acid that is required for optimal T cell activation, proliferation, and anti-tumor function. Like most proliferating cells, T cells use Gln as a building block for proteins, lipids, and nucleic acids. Tumor cells have very high proliferative rates and apart from glucose, they use large amounts of Gln for expansion. The Gln present in the tumor microenvironment (TME) is quickly used up by tumor cells and tumor infiltrating lymphocytes have to compete for this resource. Gln deficiency impairs T cell activation, proliferation, and cytokine secretion resulting in poor anti-tumor immune responses. T cells uptake Gln through the amino acid transporter ASCT2, which is a crucial mediator of Gln uptake after T cell receptor stimulation. **We hypothesized that overexpressing ASCT2 on T cells will enhance their Gln uptake in the TME further improving their function and anti-tumor immunity.** ACST2 overexpression could be an advantage for T cells in the TME, and combined with immunotherapies like chimeric antigen receptor (CAR) T cells, will enhance the efficacy of these treatments.
This project will include the use of common laboratory techniques including Molecular Biology (vector construction, cloning, qPCR), cell culture and virus production, and immunology techniques like flow cytometry, ELISPOT or ELISA. Animal tumor models will be used to test the efficacy and characterize the immune responses of ASCT2 overexpressing T cells.
The roles of the student will be:
- Construction and production of retroviral vectors able to successfully express ASCT2.
- Production of retrovirus to engineer T cells to express ASCT2. Synergic expression of ASCT2 and CARs.
- *In vitro* characterization: analyze expression and functionality of previously modified T cells using different techniques.
- *In vivo* characterization of the modified cells during anti-tumor immune response using different tumor models in mice.

yes	x
no	

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