Research Project Proposal
Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 18

Title: *New approaches of CAR-T therapy against the tumour microenvironment*

Department/ Laboratory
Immunology and Immunotherapy program
Lab 3.02. CIMA

Director 1 *Teresa Lozano Moreda*
Contact: *tlmoreda@unav.es*
Codirector: Juan José Lasarte Sagastibelza
Contact: *jjlasarte@unav.es*

Summary: Chimeric Antigen Receptor T-cells (CAR-T) is one of the most promising advanced therapies for the treatment of cancer. The current generation of CAR-T showed spectacular efficacy in certain hematological cancers. However, CAR-T was not as successful in treating solid tumours, due to several important reasons. On the one hand, it is extremely difficult to find a specific antigen for each type of tumour (TSA). On the other hand, solid cancers have multiples barriers that neutralize the function of CAR-T cells such as the complexity of the extracellular matrix and the lack of chemokines leads to an inefficient homing of T cells. Moreover, the presence of macrophages, regulatory T lymphocytes and myeloid suppressor cells and other immunosuppressive molecules.

Goal: This project will focus on two key challenges of CAR-T in solid tumours: (i) the selection of new specific antigens of the tumour microenvironment (TME), and (ii) to provide the CAR-T cells with weapons to fight against the tumour-promoting TME.

Methodology: The project includes the use of common techniques, including Molecular Biology, cell culture, virus production, animal models of cancer and immunology techniques such as flow cytometry, ELISPOT or ELISA.
The objectives are:
- Construction and production of a retroviral vector able to express a Chimeric Antigen receptor (CAR).
- Retrovirus production for engineering T cell to express the CAR.
- In vitro characterization: Analyse expression and functionality of the CAR-T cell.
- In vivo characterization of CAR-T cells and analysis of anti-tumoral activity in tumour animal model.

yes	**X**
no	

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