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

Project Nº 27
Title: *CAR-expressing macrophages as adoptive cell therapy for solid tumors*
Department/ Laboratory   *Laboratories 3.01 and 3.02. Program of Immunology and Immunotherapy, 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. Features associated with their tumor microenvironment, including the immunosuppressive milieu and the incapacity of T cells to home into tumors, have been proposed as factors responsible for this limited efficacy. Macrophages have a high capacity to infiltrate solid tumors, direct tumor phagocytosis, professional antigen presentation and activation of the tumor microenvironment. Moreover, they secrete factors that modulate the tumor extracellular matrix (ECM).

Thus, **the goal** of this project is to develop an adoptive cell therapy strategy based on the administration of macrophages modified to express CARs. Different CARs will be tested, considering as CAR targets antigens that are either expressed by tumor cells, by the ECM, or both, in order to guide macrophage homing into the tumor and to induce pro-inflammatory antitumor responses.

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 macrophage effector functions (determined by microscopy, flow cytometry, ELISA, cytotoxicity), as well as gene expression techniques (RT-PCR) will be used. Moreover, these therapies will be tested in in vivo experiments by using immunocompetent tumor models. This will help to determine their efficacy as well as associated mechanisms. For this purpose, immunological techniques including ELISPOT, flow cytometry for phenotyping and functional experiments will be used.

yes	x
no	

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