Universidad de Navarra
Facultad de Ciencias

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

Project Nº 12

Title: In vitro and in vivo validation of tumor-specific T cell receptors identified by molecular signatures. A new approach for adoptive T-cell therapy.

Department/ Laboratory *Adoptive T-cell Therapy, Immunology and Immunotherapy program, Division cancer, CIMA*

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Summary

A promising form of cancer treatment is TCR-T therapy, which consists on modifying T cells from a cancer patient with a tumor-specific T-cell receptor (TCR) to allow them to recognize and destroy the tumor. TCR-T therapy is postulated to be better suited than other T-cell therapies (such as CAR-T cell therapy) for treating solid tumors since the majority of tumor antigens are intracellular and, therefore, can only be recognized by TCRs. However, conventional methods for identifying tumor-specific T cells and their cognate TCRs are time-consuming. Recent studies show that the transcriptome of tumor-specific tumor-infiltrating T cells (TILs) is unique and different from that of irrelevant (non-tumor-specific) TILs. Our hypothesis is that the transcriptomic signature of TILs can be used as a biomarker to accurately and rapidly identify tumor-specific TCRs. Using a melanoma mouse model in which tumor-specific and irrelevant TCRs are known, we have performed single-cell RNA sequencing (scRNA-seq) and TCR sequencing (scTCR-seq) on TILs directly isolated from resected tumors and found a genetic signature that accurately identifies tumor-specific TCRs. The objective of this TFM is to evaluate the potential of this signature for the prospective identification of tumor-specific TCRs in a previously uncharacterized mouse model of breast cancer. The project will involve the use of many different techniques including: molecular biology, retrovirus production, T-cell genetic modification, in vitro tumor-reactivity assays, flow cytometry analysis, breast cancer mouse models, in vivo experiment to evaluate the antitumor efficacy of TCR-T cells and monitor the immune responses, interpretation of single-cell sequencing data, etc.

yes	x
no	

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