



Research Project Proposal

Academic year 2019-2020

Project Nº 31

Title:

Effect of the activation of key molecules for the survival and metabolic fitness of T cells to enhance their antitumor efficacy

Department/ Laboratory

Program of Immunology and Immunotherapy (CIMA)

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Summary

Immunotherapy is a type of cancer treatment that boosts the body's natural defenses to fight cancer. The proliferation, effector functions and survival of tumor-infiltrating lymphocytes (TILs) determine, to a large extent, the efficacy of immunotherapy against cancer. Recent studies show that **CD8 T cells undergo apoptosis within the tumor microenvironment**, suggesting that their apoptosis could be a mechanism that limits the capacity of the immune system to reject tumors. On the other hand, the TILs are at a clear **metabolic disadvantage** with respect to tumor cells, competing with them for nutrients and oxygen, which limit their proliferation and effector functions. In order to potentiate the antitumor efficacy of TILs, in this project we will study different immunotherapy strategies aimed to **make CD8 TILs more metabolically competitive**, as well as **to slow down their apoptosis**.

For that purpose, the following objectives are proposed:

*Study the effect of the **activation of key molecules for the survival and metabolic fitness of T cells to enhance their antitumor efficacy***

- Analysis, by flow cytometry, of the impact of the treatments on the effector functions, number and apoptosis of TILs.
- Study, by analysis of RNAseq, of the effect of the treatments on the gene signature of TILs.
- Study of the mitochondrial respiratory capacity, ATP production and Glycolysis pathway.

The project will involve the use of many different techniques, including: animal models of cancer, analysis of protein expression by flow cytometry, analysis of RNAseq and Gene Set Enrichment Analysis (GSEA), and bioenergetic analysis.

yes	<input checked="" type="checkbox"/>	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	<input type="checkbox"/>	