

Research Project Proposal

Project Nº 16
Title: Adoptive Immunotherapy of Cancer with Tumor-infiltrating T Lymphocytes (ACT-TIL): selection of tumor-specific T cells to enhance their therapeutic effectiveness.
Department/ Laboratory Regulación de la Respuesta Inmune Adaptativa, Programa de Inmunología e Inmunoterapia, CIMA
Director 1 Sandra Hervas-Stubbs Contact: mshervas@unav.es
<p>Summary:</p> <p>Adoptive immunotherapy (ACT) of cancer with tumor-infiltrating T lymphocytes (TILs) is emerging as a curative therapy for advanced cancer⁽¹⁻²⁾. T lymphocytes are the most effective cells fighting cancer but, after repetitive exposure to tumor cells, they become exhausted and senescent. ACT-TIL consists on collecting TILs from the tumor of the patient and growing them in the laboratory. This process rescues cells with proliferative potential and also reverses T-cell exhaustion. Expanded TILs are given back to the patient to help the immune system fight disease. TILs can be grown from varied cancers but they rarely demonstrate high antitumor reactivity. Using sensitive techniques rare populations of TILs with high tumor specificity have been identified in several types of tumors. These tumor-reactive cells can be distinguished by the expression of certain markers associated to T-cell activation⁽³⁾. These molecules could be used to isolate these low-frequency T-cell populations. Our goal is to improve the antitumor efficacy of ACT-TIL through the selection of tumor-specific TILs on the basis of the expression of surrogate biomarkers of tumor specificity, such as costimulatory (OX40/ICOS/CD137/GITR...) and inhibitory (PD1/CTLA4/LAG3/TIM3...) molecules, which are normally expressed by recently activated or tumor-experienced T cells. Thus, different populations of TILs will be isolated by flow cytometry. Selected TILs will be expanded in the lab and their antitumor specificity and therapeutic activity will be verified in vitro and in vivo. This study will allow the identification of the set of biomarkers that best serve to isolate the repertoire of tumor-specific TILs for therapeutic use.</p> <p>References</p> <p>(1) Rosenberg SA, Restifo NP. Adoptive cell transfer as personalized immunotherapy for human cancer. <i>Science</i>. 2015; 348(6230):62-8.</p> <p>(2) Hinrichs CS1, Rosenberg SA. Exploiting the curative potential of adoptive T-cell therapy for cancer. <i>Immunol Rev</i>. 2014; 257(1):56-71.</p>



(3) Ye Q, Song DG, Powell Jr DJ. Finding a needle in a haystack: Activation-induced CD137 expression accurately identifies naturally occurring tumor-reactive T cells in cancer patients. *Oncoimmunology*. 2013; 2(12):e27184.

POSSIBILITY OF PhD

YES*

* (PhD grant required)