Research Project Proposal
Academic year 2018-2019

Project Nº 27

Title: Characterization *of T regulatory inhibitors for Immunomodulation in anti-tumour treatments.*

Department/ Laboratory
Immunology and Immunotherapy program
Lab 3.02. Immunomodulation Therapy
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Summary.
Although T regulatory cells (Treg) are essential for the prevention of autoimmune diseases, their immunoregulatory function restrains the induction of immune responses against cancer or chronic inflammation. Thus, development of inhibitors of FOXP3, a key transcription factor for the immunosuppressive activity of Treg, might give new therapeutic opportunities. In a previous work we identified two peptides (named optimized P60 or Fx393-403) able to enter into the cells, bind to FOXP3 or NFAT respectively, and impair Treg activity *in vitro* and *in vivo*. In this project, we are interested in doing further analysis to characterize the impact of these inhibitory peptides alone or in combination with other current therapies in different tumour models and also in antibody production. The results of this project can then be used to improve anti- tumour therapies based on immunomodulation.

Goal
Evaluate the therapeutic role of regulatory T cell inhibition to enhance immune response and antibody production.

Methodology.

1. Effect of Treg inhibition in anti-tumor vaccines: Analysis of immune response.
    - Vaccination with different tumour antigens, such as AH1, AFP, OVA epitopes in combination with our Treg inhibitory peptides
    - Combination of vaccination strategies, Treg inhibition and immuno-checkpoint inhibitors to find the best therapeutic strategy.
    - To characterize the anti tumourimmune response using techniques such as ELISPOT, flow cytometry and ELISA.

2. Effect of Treg inhibition in antibod generation. To evaluate the impact of Treg inhibition in antibody production, , mice will be vaccinated with OVA protein and complete Freund´s adjuvant (CFA) in combination with our inhibitory peptides at day 0, 15, 30 and 45. Serum samples will be collected at day 30 and 45 to quantify the OVA antibody titres by ELISA.

3. Effect of Treg inhibition in anti-tumor therapy. Finally, we will evaluate Treg inhibitory activity in different tumour models:
   - First, we will characterize the immune phenotype of these tumour models (colon: CT26, melanoma: B16OVA, breast: TC-1, lung: LLCOVA) by flow cytometry.
   - Second, evaluate the therapeutic effect of Treg inhibition alone or in combination with a-PD1, aCTLA4 or chemotherapy (Cisplatin).
   - Then, we will try to find some correlation between the efficacy of our peptides with the tumour immune phenotype.

yes	**x**
no	

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