Universidad
de Navarra
Facultad de Ciencias

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

Project Nº 34
Title: Identification of neoantigens in multiple myeloma to develop personalized vaccines
Department/ Laboratory   *Laboratories 3.01. Program of Immunology and Immunotherapy, CIMA.*
Director 1 *Diana Llopiz*   **Contact:** *diallo@unav.es*   **Codirector:** *Pablo Sarobe*   **Contact:** *psarobe@unav.es*
Summary   Neoantigens (neoAgs), new sequences originated from tumor mutations, may induce potent tumor-specific T cell responses. The mutational level and the concomitant neoAg load are associated with response rate to immunotherapy in many tumors. In the case of multiple myeloma (MM), the tumor mutational burden is intermediate, but recent studies identified the presence of neoAgs in these patients. Vaccination may help to increase antitumor immunity, which can be later combined with other immunotherapies. Thus, in order to develop future combinatorial protocols for MM patients, the **goal** of this project is the identification of neoAgs in two preclinical models of MM, characterization of their immunogenicity and validation of their therapeutic capacity when included in vaccines. To achieve this goal the following **methodology** will be used: First, from data obtained in whole exome sequencing studies, potential neoAgs will be selected by using bioinformatic algorithms predicting binding to MHC molecules. Highly-ranked mutated peptides will be tested in vitro by flow cytometry, to measure its binding capacity to MHC molecules. Binder peptides will be used to immunize mice, to demonstrate their immunogenicity by using T cell functional assays (Elispot, flow cytometry, Elisa), phenotyping methods (flow cytometry), cytotoxicity and antigen presentation assays. Next, polyepitopic vaccines containing immunogenic peptides will be administered to mice with established MM tumors, to determine vaccine efficacy and the underlying mechanisms responsible for this activity. This will include cell depletion experiments, analysis of immune parameters by Elispot, flow cytometry, ELISA, RNAseq, with the help of bioinformatic analytical tools

yes	**X**
no	

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