Research Project Proposal
Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 27

Title:
New antigen targets for vaccination in hepatocellular carcinoma: identification of T cell epitopes from micropeptides derived from long non-coding RNAs

Department/ Laboratory.
Immunology and Immunotherapy Program. Lab 301. CIMA
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Summary

Despite the success of checkpoint inhibitors for cancer immunotherapy, there is still a proportion of patients that do not respond to this treatment. To increase the rate of response to checkpoint inhibitors combinatorial strategies should be used, such as to generate new antitumor T cells with vaccines aimed at inducing T cell immunity. However, vaccines require the use of proper tumor antigens, with high immunogenicity and tumor specificity. In the field of hepatocellular carcinoma (HCC), we have identified several long non-coding RNAs (lncRNA) over-expressed in a high proportion of tumors and in testis (an immune-privileged site), predicted to encode for short micropeptides. This tissue expression pattern suggests that these peptides could be considered as tumor antigens. Thus, the main goal of this project is the identification of T cell epitopes in HCC micropeptides and the characterization of their immunogenicity, to be used as antitumor vaccines. The project will involve transcriptome analyses of lncRNAs in HCC samples, in silico prediction of translation and binding to MHC molecules of peptides encoded by these lncRNA, experimental in vitro testing of this predicted binding, and in vivo characterization of peptide immunogenicity in transgenic mice expressing human MHC molecules. This will be based on the use of sequence analyses (coding potential, ribosome profiling, mass spec databases) and MHC binding algorithms, cellular in vitro assays and classical immunology assays measuring T cell phenotype and functions like ELISPOT, ELISA, flow cytometry, cell proliferation and tumor killing capacity. Our goal is to develop strategies with clinical translation for the treatment of patients with HCC.

yes	**x**
no	

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