Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2025-2026

Project Nº 11
Title: Identification of neoAgs in hepatocellular carcinoma to develop neoAg-based immunotherapies
Department/ Laboratory *Laboratory 3.01. Program of Immunology and Immunotherapy, CIMA.*
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Summary Immune checkpoint inhibitor (ICI)-based immunotherapy in hepatocellular carcinoma (HCC) promotes clinical responses only in 30% of patients. Neoantigens (neoAgs) are mutated sequences expressed by tumor cells that can be recognized as foreign by lymphocytes and induce tumor rejection. NeoAg load positively correlates with efficacy of ICI and adoptive T cell-based therapies, suggesting that promoting neoAg-specific immunity would help immunotherapy efficacy. To design these new therapies, a solid preclinical basis is required to support the subsequent use of these strategies in patients. Currently, there are no HCC animal models to test neoAg-based therapies, due to the lack of information on the neoAg repertoire in murine HCC. Thus, the main **goal** of the project is the identification of neoAgs in two mouse HCC models for subsequent development neoAg-based therapies. **Methodology** will include cell cultures, generation of murine HCC tumors, analysis of sequencing data, neoAg prediction and analysis of neoAg immunogenicity (immunization, in vitro studies of T-cell activation, including cytokine production by ELISPOT, ELISA and intracellular cytokine detection by flow cytometry). Activity of neoAg-specific T-cells will be tested in vitro against peptides and against tumor cells in co-cultures measuring T-cell activation by multiparametric flow cytometry, tumor cell lysis and inhibition of tumor cell proliferation. Selected neoAgs will be incorporated into tumor model-specific vaccines to test their efficacy in vivo in tumor-bearing mice, either as monotherapies or in combination with currently approved ICI. Mechanisms of response to therapies will be studied using tumor samples from treated mice by flow cytometry and immunohistochemistry.
<table><tr><td>yes</td><td>x</td></tr><tr><td>no</td><td></td></tr></table>Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?