



MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2023-2024

Project Nº 35

Title: Identification of immunotherapeutic combinations for the treatment of hepatocellular carcinoma

Department/ Laboratory

Laboratory 3.01. Program of Immunology and Immunotherapy, CIMA.

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Summary Short summary of the project with a maximum extension of 250 words, including the goals and the methodology that will be used

Despite important advances of immunotherapy in hepatocellular carcinoma (HCC) patients, an important proportion of individuals do not respond to these treatments. Differences in the tumor immune microenvironment between patients suggest that therapies should be tailored according to the presence of cellular and molecular targets in each tumor. Thus, in addition to commonly used checkpoint inhibitors (ICI), new drugs should be incorporated to design more potent combinations for non-responder patients according to their immunotype.

Thus, the goal of this project is the identification of new immunotherapeutic combinations to increase the rate of response to HCC. Different combinations including ICI plus other compounds will be tested in order to identify their activity in different tumor types. Methodology will include generation of different murine tumors, ex vivo culture of tumor explants with a panel of immunotherapeutic drugs and characterization of immune activity upon culture of stimulated tumor tissue with combined therapies. This will include analysis of soluble factors by multiparametric assays and by ELISA, characterization of infiltrating immune cells (numbers, phenotype and functional properties) by flow cytometry, and gene expression analyses by RNA-seq and RT-PCR. Activity of successful combinations will be further tested in vivo, by administering selected drugs to mice bearing hepatic tumors where, in addition to determine their therapeutic efficacy, associated immune effects will be characterized. Finally, to confirm the translatability to the human setting of combinations yielding clear in vivo therapeutic effects in murine models, they will be tested in vitro by using tumor explants obtained from HCC patients.

Table with 2 columns and 2 rows: yes, x; no,

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