Universidad de Navarra
Facultad de Ciencias

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

Project Nº 18

Title: Actionable neutrophil-associated mechanisms in immunotherapy that interfere with T-cell crosspriming in the tumor microenvironment

Department/ Laboratory *Immunology and immunotherpay department. Laboratorio de estrategias de inmunoterpia traslacional.*

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Summary.

Neutrophils constitute one of the first lines of defense against microbial pathogens, but their functions are usually co-opted by cancer to favor tumor progression, metastases and suppress anti-tumor immune responses. Type I conventional dendritic cells (cDC1) present in tumors are able to cross-present antigens to CD8 T cells allowing effective antigen-specific anti-tumor immune cytotoxic responses. As a consequence, the abundance of cDC1 cells within tumor tissue strongly correlates with longer overall survival and more favourable objective responses to immunotherapy in cancer patients. On the contrary, the presence of neutrophils usually correlates with poor prognosis and lack of clinical responses to immune checkpoint blockade-based immunotherapy. The Msc candidate will study the potential relation of these two mechanims, namely neutrophil infiltration and crosspiming, in cancer bearing hosts. Our hypothesis is that neutrophils impair antigen crosspriming resulting in weaker anti-tumor immune responses. By using in vivo models of cancer and ex vivo cocultures of these populations, the MSC project will address the potential impact that tumor associated neutrophils have on cDC1 infiltration, maturation and crosspriming functions. Flow cytometry and multiplex tissue immunofluorescence will be used to define the spatial relationship between these two leukocyte populations. Therapeutic interventions to limit neutrophil infiltration and promote tumor antigen crosspriming will be experimentally developed and its impact in poorly immunogenic tumor models will be studied in combined immunotherapy strategies. Ideally, the successful candidate should have previous cell culture/microscopy and mouse experimentation experience to fit with the objectives of this research project.

yes	X
no	

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