

Research Project Proposal
Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 55	
Title Adjuvant treatment with anti-VEGFR3 to improve success of immunotherapy in breast cancer	
Department/ Laboratory Department of Biochemistry and Genetics and Immunotherapy group at CIMA	
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Summary. <p>Breast cancer malignancy is strongly associated to the establishment of metastases to the regional lymph nodes and distant organs. Breast tumors produce the lymphangiogenic molecule VEGF-C that signals through VEGFR3 receptors. In tumors, excessive VEGFR3 signaling associates with lymphatic metastases, impaired immune cell migration and a shift of tumor infiltrating myeloid cells towards suppressor phenotypes. Current efforts in improvement of breast cancer treatment include immunotherapy with inhibitors of the immune checkpoint (ICPI) with discrete results, mostly due to stroma-derived immune-suppression.</p> <p>Here, we propose targeting the VEGFR3 pathway concomitantly to immunotherapy to improve responses by alleviating myeloid-derived immune-suppression. We will approach this concept by interrogating a cohort of patients along with modelling breast cancer in mice.</p> <p>Concretely, we will pursue the following specific objectives:</p> <ol style="list-style-type: none"> 1- Analysis of the relationship between the expressions of lymphedema-associated genetic signatures and responses to therapy in clinical samples obtained from breast cancer patients. 2- To study the modulatory effects of VEGFR3 inhibition in the immediate response to immunotherapy in pre-clinical models of breast carcinoma, in terms of: <ul style="list-style-type: none"> Survival, tumor growth and onset of lymph node and distal metastases Modulation of the tumor immune phenotype and cytotoxic activity Stabilization of the tumor associated lymphatic vasculature Migration of myeloid cells to adjacent lymph nodes 3- Examination of distal responses. We will study: <ul style="list-style-type: none"> Immunological memory after resection of the primary tumor and posterior re-challenge. Effects of the depletion of the myeloid compartment <p>Looking for ways to minimize immune-suppression during treatment would be of great benefit to the patient.</p>	
yes	X
no	
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?	