Research Project Proposal
Academic year 2021-2022

Máster en Investigación Biomédica

Project Nº 37	
Title Adjuvant treatment with anti-VEGFR3 to improve success of combined radio- and immunotherapy in breast cancer	
Department/ Laboratory *Department of Biochemistry and Genetics (UNAV) and Immunotherapy group at CIMA*	
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Summary.

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 (IChPI) with discrete results, mostly due to stroma-derived immune-suppression.

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.

Concretely, we will pursue the following specific objectives:
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 myeloid pro tumor in two pre-clinical models of breast carcinoma (E0771 and 4T1 tumors), in terms of:
       Survival, tumor growth and onset of lymph node and distal metastases
       Modulation of the tumor immune phenotype and cytotoxic activity
       Migration of myeloid cells to adjacent lymph nodes
3- Study of *in vivo* migration of immune cells by use of kikume photoconvertible-mice

Looking for ways to minimize immune-suppression during treatment would be of great benefit to the patient.

yes	X	**Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?**
no		