



MÁSTER EN INVESTIGACIÓN BIOMÉDICA

Research Project Proposal

Academic year 2022-2023

Project Nº 52	
Title: <i>Pit-stop in cancer immunotherapy: conditioning tumor microenvironment by selective targeting tumor associated macrophages</i>	
Department/ Laboratory <i>CIMA Immunotherapy and Department of Biochemistry and Genetics</i>	
Director 1 <i>Ana Rouzaut</i> Contact: <i>arouzaut@unav.es</i>	
Summary. <p>Cancer Immunotherapy has already gained a prominent role in the treatment of cancer, being check point inhibitors the most promising therapeutic weapon developed so far. Nevertheless, it is frequent to encounter innate or acquired resistances to immunotherapy. Development of an immune suppressive environment constitutes one of the cancer-evasion strategies. Tumor associated macrophages (TAM) can appear in two different flavors: inflammatory with mostly an anti-tumoral activity (M1) or immune-suppressive (M2) with pro-tumoral activity. Both phenotypes are dynamic and depend on the cytokines and growth factors present in the tumor microenvironment.</p> <p>The receptor for the vascular growth factor C, VEGFR3, besides participating in lymphatic endothelial cell development and growth, is expressed by tumor macrophages with immune suppressive functions. In fact, treatment with antagonists of this receptor switch their phenotype from immune suppressive to pro-inflammatory phenotypes.</p> <p>In this project, we want to study whether pre-treatment with the VEGFR3 inhibitor SAR131675 before immunotherapy induces M2 to M1 TAM phenotype switch, improves anti-tumor cytotoxicity and survival. SAR131675 has a lipidic nature. Therefore, its solubility in serum is very low. To overcome this problem, we will produce VEGFR3-loaded nanoparticles directed towards by macrophages. Tissue distribution and macrophage incorporation will be studied by fluorescent labelling of the nanoparticle and scan analysis.</p> <p>To test the efficacy of the SAR-nanoparticles, we will compare tumor size, immune infiltration and survival of mice inoculated with breast cancer tumors and pre-treated with SAR131675 intraperitoneally or with VEGFR3-loaded nanoparticles before receiving immunotherapy with immune check-point inhibitors.</p> <p>The goal of this project is double: to improve cancer treatment and to develop drug carrier particles attractive to the Pharmaceutical Industry.</p>	
yes	X
no	
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?	