



Research Project Proposal
Academic year 2021-2022
Máster en Investigación Biomédica

Project Nº 26		
Title: <i>The role of the STING pathway in the mechanisms involved in anti-PD-1 treatment resistance in patients with STK11/LKB1 mutant NSCLC</i>		
Department/ Laboratory Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc. <i>Department of Oncology (CUN)/Laboratorio de Marcadores predictivos de respuesta (CIMA). 2.01</i>		
Director 1: Ignacio Gil Bazo Contact: igbazo@unav.es		
Summary: Immunotherapy options as new therapeutic strategies against solid tumors have recently emerged and demonstrated a clear benefit in terms of survival and quality of life. More specifically, in patients with Non-Small Cell Lung Cancer (NSCLC), concurrent mutations in KRAS and TP53 have shown to confer a greater sensitivity to anti-PD-1/PD-L1 monoclonal antibodies. However, when KRAS mutations are present concurrently with STK11/LKB1 mutations, immunotherapy treatments seem not to benefit NSCLC patients and their prognosis is dismal. Recently, several investigations have shown that LKB1 loss may directly drive to the suppression of the stimulator of interferon genes (STING) and the lack of detection of the cytoplasmic double-stranded DNA leading to immune escape. Similarly, we have found that the inhibition of Inhibitor of Differentiation-1 (Id1), favors the immune response through the immune system activation. Among Id1 high-expressing KRAS mutant lung cancers, STK11 mutations are frequent. The use of different strategies directed to reactivate STING along with Id1 inhibition, may rescue the sensitivity of anti-PD-1 therapies in different lung cancer murine models, through a significant tumor antigens detection by the immune system. In this project, we aim to study the correlation between the STING pathway and STK11/LKB1 mutations according to Id1 expression levels and how Id1 blockade may help to induce tumor sensitivity to anti-PD-1 therapies in different murine xenograft and metastatic models of lung cancer.		
yes	<input checked="" type="checkbox"/>	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no	<input type="checkbox"/>	