



Research Project Proposal

Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 38		
Title: <i>New therapeutic combinations against KRAS-driven non-small cell lung cancer (NSCLC). Study of new biomarkers of response to anti-PD-1 therapy.</i>		
Department/ Laboratory <i>Department of Oncology (CUN)/Laboratorio de Marcadores predictivos de respuesta (CIMA). 2.01</i>		
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Summary <p>In this study, we plan to demonstrate that targeting <i>Id1</i> gene in different <i>KRAS</i>-driven murine models of lung cancer has an immunostimulatory role that favours the activation of different immune populations. In addition, we intend to study that the inhibition of <i>Id1</i> expression, both in the tumor immune microenvironment and in tumor cells (by silencing <i>Id1</i> using short hairpin RNA or by using a small inhibitory molecule), combined with PD-1 blocking (using specific monoclonal antibodies) and MEK1/2 (with last-generation inhibitors) represents a synergistic antitumor strategy in <i>KRAS</i> driven NSCLC. Furthermore, we want to explore the influence not only of the <i>KRAS</i> status but also the role of concurrent mutations in TP53 and LKB1/STK11 in the clinical evolution of a prospective series of 50 consecutive patients with advanced NSCLC treated with monoclonal antibodies against PD-1. We also plan to study the predictive role of response to PD-1 inhibitors by analyzing the combined expression, by immunohistochemistry, of <i>Id1</i> and PD-L1 in the tumor samples of those patients and their correlation with the presence or absence of mutations in <i>KRAS</i> and the concurrence of those, with genomic alterations in TP53 and/or LKB1/STK11. Other potential predictive biomarkers such as the presence of TIL and the combined expression of other immune activation markers (CD4, CD8, CD3, FOXP3, CD68, PD-1, PD-L1, CD11b, CD56 and CD16), will be investigated by multispectrum immunophenotyping as well as the role of secreted soluble cytokines. Finally, we will investigate the mechanisms by which <i>Id1</i> acts blocking the activation of the immune response, by studying <i>in vitro</i> its role in peripheral blood lymphocytes and antigen-presenting cells.</p>		
yes	X	Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?
no		