



Research Project Proposal
Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 47	
Title: <i>Development of novel strategies to potentiate lung cancer immunotherapy</i>	
Department/ Laboratory <i>Program in Solid Tumors (CIMA).</i>	
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<p>Summary Immunotherapy based on PD-1/PD-L1 blockade has emerged as a potent tool for the treatment of lung cancer. These drugs remove the inhibition of T-cell activation and restore antitumor immune responses. However, PD-1/PD-L1 inhibition is not capable of reversing all resistance mechanisms, and a proportion of patients do not respond adequately to PD-1/PD-L1 immunotherapies. We have demonstrated that the inhibition of the C5a/C5aR1 pathway synergizes with PD-1 blockade to inhibit lung cancer progression (Ajona et al. <i>Cancer Discovery</i> 2017), and the metastatic spread (Ajona et al. <i>AJRCCM</i> 2018). In this context, a Phase I/II study (STELLAR-001) is now evaluating the safety and efficacy of combined inhibition of C5a/C5aR1 and PD-1/PD-L1 signalling in patients with advanced solid tumors. Moreover, in a recent study, we have shown that short-term starvation (STS) sensitizes lung tumors to PD-1/PD-L1 blockade (Ajona et al. <i>Nature Cancer</i> 2020). Mechanistically, C5a/C5aR1 blockade and STS affect different pathways of the tumor microenvironment (MDSCs and Treg cells, respectively). Therefore we here propose a project in which the mechanisms that mediate the effect of C5a/C5aR1 and STS in lung tumors will be studied. Moreover, we will dissect the immunological effects of the combined therapy anti-C5a/STS/PD-1 in syngeneic <i>in vivo</i> models in order to optimize this therapy and overcome the resistance mechanisms. This project will contribute to a better knowledge of the interaction between cancer and the innate immunity, will provide insights into new therapeutic targets, and may provide support for the development of new therapies against lung cancer.</p>	
yes	X
no	
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?	