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

Project Nº 19 ASIGNADO

Title:
Role of YES1 in small cell lung cancer

Department/ Laboratory where the project will be carried out indicating Department, Area, Faculty, CUN, CIMA etc.
Program in Solid Tumors, CIMA, Laboratory 202.

Director 1: **Alfonso Calvo González** (If there will be two co-directors indicate both)
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Summary:

Small Cell Lung Cancer (SCLC) accounts for 15% of all lung cancer patients and constitutes a recalcitrant tumor with a very poor prognosis. The therapeutic regimens involve chemo- and radiotherapy, but the rapid emergence of resistance and metastases explain its poor survival rates (~7%). Based on its high mutational load, SCLC represents a candidate for immunotherapeutic-based strategies. However, the clinical response to ICIs is much less pronounced than that of non-small cell lung cancer (NSCLC), probably due to an uncharacterized tumor immunosuppressive microenvironment. Therefore, there is an urgent need to develop novel strategies to treat SCLC.

In NSCLC we have previously demonstrated that YES1 is a novel therapeutic target and that genetic amplification/overexpression of YES1 is an accurate biomarker of response to dasatinib. Moreover, in a recent publication we have demonstrated that dasatinib synergizes with anti-PD-1 in animal models of NSCLC to produce tumor regressions and immunological memory. Based on this information we decided to investigate whether YES1 could also constitute a target and biomarker in SCLC. The master's project will be part of an ongoing research in the Lab, where we have found that YES1 is amplified and overexpressed in a subset of SCLC and that targeting YES1 pharmacologically impairs significantly tumor growth. Specifically, the goals of the project will be: 1) to study molecular mechanisms of YES1 in SCLC; 2) to assess if the combination of YES1-targeting drugs and anti-PD-1 also causes tumor regressions in SCLC; 3) to determine if YES1 can be considered as a biomarker of response.

The candidate will learn molecular and cellular techniques, such as cell culture, western blot, PCR, flow cytometry, immunofluorescence and immunohistochemistry. He/she will participate in animal work related to novel immunotherapy by combining YES1 inhibitors and anti-PD-1. The project will be carried out with help of members of the laboratory and results will be discussed in group meetings.

yes	X
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?