



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

Project Nº 18 ASIGNADO

Title: **Novel strategies to overcome immunotherapy resistance in NSCLC**

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**

Contact: acalvo@nav.es

Codirector: Francisco Expósito

Contact: fran.exposito.rincon@gmail.com

Summary: Non-small Cell Lung Cancer (NSCLC) accounts for 85% of all lung cancer patients and is usually diagnosed at late stages. Survival rates are still below 20%, which shows the need of investigating novel therapeutic strategies. Immunotherapy have changed dramatically the management of NSCLC patients, with pembrolizumab, nivolumab and atezolizumab as approved antibodies that block the PD-1/PD-L1 axis, for the treatment of patients with advanced disease. However, resistance mechanisms eventually occur. Different mechanisms have proven to confer primary or acquired resistance, such as mutations in B2M, the loss of HLA, the coexistence of *KRAS* and *STK11* (LKB1) mutations, the gain in Myc expression, etc.

Using CRISPR/Cas9 technology we have developed NSCLC models with resistance to anti-PD-1 therapy by targeting B2M. The master's project will be intended to characterize these models and to test novel strategies based on immunotherapy to overcome such resistance. Specifically, these are the goals: 1) to determine in vitro whether our cancer cells lacking B2M cannot present antigens; 2) To characterize the immune microenvironment of B2M knock out tumors in comparison with tumors with wild type cells; 3) to test a variety of novel therapies in these models with the aim of overcoming resistance to anti-PD-1.

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

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| yes | X |
| no | |

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