

Research Project Proposal
Academic year 2016-2017

Project Nº 2
Title: Preclinical evaluation of anti-PD-L1 in combination with lenalidomide for the treatment of leukemia, lymphoma and myeloma
Department/ Laboratory Flow cytometry core – CIMA LAB Diagnostics, Center for Applied Medical Research (CIMA)
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<p>Summary</p> <p>Although results using checkpoint inhibitors are highly promising in solid tumors, there is significantly less data available in hematological malignancies. Accordingly, several correlative biomarkers have already been identified to predict the efficacy of anti-PD-L1 and/or anti-PD-1 based-therapies in NSCLC, RCC or melanoma but not in leukemia, lymphomas, and myeloma. We hypothesize that a better understanding of the cellular and molecular basis of anti-PDL1 MoAbs in primary samples representative of different haematological malignancies could help to unravel biomarkers for prospective identification of patients who are likely to respond to the drug but also to monitor drug efficacy, and to provide biological rationale to further support blocking the PD-1/PD-L1 axis in combination with IMiDs for the treatment of MDS, AML, B-CLPD and MM.</p> <p>Specific Aims:</p> <p>Aim 1: To determine PD-1 and PD-L1 surface expression on normal and tumour cells from primary bone marrow (BM) samples from patients with MDS, AML, B-CLPD and MM using multidimensional flow cytometry.</p> <p>Aim 2: To evaluate using multidimensional flow cytometry the ex vivo efficacy/toxicity profile of anti-PD-L1 in combination with lenalidomide, pomalidomide or CC-122 in primary samples from patients with AML, B-CLPD and MM, as well as their combined effect in immune cells in MDS, AML, B-CLPD and MM.</p> <p>Aim 3: To define the immune cells responsible for drug efficacy and to understand the molecular mechanisms behind tumor chemoresistance to anti-PD-L1 in combination with lenalidomide or CC-122</p>



POSSIBILITY OF PhD :YES*

* (PhD grant required)