

Research Project Proposal
Academic year 2016-2017

Project Nº 4
Title: Therapeutic effect of a combined strategy to block PD-1 and Id1 in a murine model of lung cancer
Department/ Laboratory Laboratory 1.02 Center for Applied Medical Research (CIMA)
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<p>Summary</p> <p>Inhibitor of Differentiation-1 (Id1) is a gene involved in tumor differentiation, proliferation, angiogenesis, drug-resistance, migration and metastasis (1). Interestingly enough, Id1 inhibition in different animal models has shown promising therapeutic results. More recently, it has been postulated that Id1 may also play a critical role in suppressing the anti-tumor immune response during tumor progression and metastasis through downregulation of molecules involved in dendritic cell differentiation and suppression of CD8 T-cell proliferation (2). The therapeutic paradigm of lung cancer, the principal cause of death by cancer worldwide, has dramatically changed with the clinical demonstration of the high antitumor efficacy shown by the immune checkpoint blockers Nivolumab and Pembrolizumab (monoclonal antibodies against PD-1) (3).</p> <p>Combination strategies adding PD-1 blockers (Nivolumab or Pembrolizumab) to standard chemotherapy or antiangiogenic or targeted therapies are under evaluation with preliminary promising results.</p> <p>However, a potential combination of Id1 and PD-1 inhibition has never been tested. We aim to demonstrate that the combined inhibition of Id1 in lung cancer tumor cells and the immune modulation through PD-1 inhibition in the tumor and the tumor immune microenvironment has a synergistic antitumor effect.</p> <p>We will use the murine lung cancer cell line Lewis Lung Carcinoma (LLC) in immunocompetent mice to create both, a metastatic model as well a xenograft model. After Id1 wild-type and Id1 knock-down tumor cells inoculation, mice will be treated with a PD-1 inhibitor (Nivolumab) or placebo. The therapeutic efficacy will be measured according to the genomic background of the LLC injected and the treatment provided.</p> <p>References</p> <p>1. Perk J, Iavarone A, Benezra R. Id family of helix-loop-helix proteins in cancer. <i>Nat Rev Cancer</i>. 2005 Aug;5(8):603-14. Erratum in: <i>Nat Rev Cancer</i>. 2005 Sep;5(9):750.</p>



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POSSIBILITY OF PhD YES*

* (PhD grant required)