



Research Project Proposal
Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 08	
Title: <i>Novel epigenetic strategies for the treatment of liver tumors.</i>	
Department/ Laboratory: <i>Hepatology Program. CIMA.</i>	
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Summary <p>Liver diseases cause about 2 million deaths per year worldwide. Half of these deaths are directly attributable to liver tumors (LTs), mainly hepatocellular carcinoma (HCC), but also cholangiocarcinoma (CCA) and hepatoblastoma (HB). The prevalence of the risk factors underlying these cancers is globally increasing. Therapeutic alternatives for LTs are few and most are not applicable in the advanced disease, when most cases are diagnosed. In spite of significant improvements over the past years, the efficacy of systemic therapies is still limited. Therefore, novel therapeutic strategies are needed for LTs. Epigenetic mechanisms controlling gene expression are profoundly dysregulated in cancer, including hepatobiliary tumors. These mechanisms are increasingly recognized as druggable processes with fewer toxic effects than initially anticipated, and high antitumoral efficacy. Our recent findings, and the preliminary results have demonstrated the antitumoral efficacy of the combined inhibition (either genetic or pharmacological) of epigenetic effectors such as DNA-methyltransferases and the histone-methyltransferase G9a for the treatment of experimental hepatic tumors. We have developed a new type of dual inhibitors of DNMTs/G9a, first-in-class and with an excellent toxicological profile. The aims of this project are:</p> <ol style="list-style-type: none"> 1. Explore the antitumoral mechanisms of these new type of compounds in LT cell lines. 2. Evaluate the potential af dual G9a/DNMT inhibition for the sensitization of LTs cells to chemotherapeutic agents ("episensitization" strategies). <p>The methodology implemented will include: cell culture, analysis of gene expression (qPCR and western blot), analysis of epigenetic marks in histones and DNA, pharmacological studies (drugs combinations).</p>	
yes	
no	X
Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?	