

Research Project Proposal
Academic year 2015-2016

Project Nº 13
Title: Identification of long noncoding RNAs involved in the progression of hepatocellular carcinoma
Department/ Laboratory Gene therapy and Hepatology Lab 406. CIMA
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Summary <p>Hepatocellular carcinoma (HCC) is the third cause of cancer-related death worldwide. Only ~35% of the patients with HCC are eligible for curative treatments, and most of them have a high frequency of tumor recurrence. Sorafenib is the only option for patients with advanced HCC, but sorafenib treatment increases overall survival for only three months. Therefore, there is an urgent need to develop alternative treatments for HCC. Sorafenib and most of the drugs developed in the last years, target proteins implicated in a given disease. However, out of the 90000 genes just identified in the human genome, most (almost 60000) correspond to genes that do not encode for proteins. Instead, they transcribe for long noncoding RNAs (lncRNAs). Although the function of most lncRNAs is presently unknown, some lncRNAs have been implicated in the initiation and progression of several diseases, including cancer. Nevertheless, lncRNAs have not been used as therapeutic targets. We propose to identify lncRNAs involved in the development HCC and to test the therapeutic efficacy of antisense drugs (ASOs) that target the expression of these lncRNAs. To this aim, we have identified a collection of lncRNAs upregulated in HCC and related to tumor prognosis. We will inhibit the expression of these lncRNAs with ASOs to evaluate their role in cell proliferation and the therapeutic potential of the ASOs in cell culture and in vivo. We believe that ASO-targeting of lncRNAs in the liver will represent an innovative technology for the treatment of HCC an other highly prevalent liver diseases.</p>
References <p>Reig M y cols. Systemic treatment. <u>Best Pract Res Clin Gastroenterol.</u> 2014; 28:921-35.</p> <p>Colnot S, Fortes P. Editing liver tumours. Gut 2014; 63:709-10.</p> <p>Iyer MK et al. The landscape of long noncoding RNAs in the human transcriptome. Nat Genet 2015;47: 199-208.</p>



POSSIBILITY OF PhD

YES*

* (PhD grant required) If a PhD grant is obtained