Máster en Investigación Biomédica

Facultad de Ciencias

Research Project Proposal
Academic year 2017-2018

Project Nº 8
Title: Functional analysis of noncoding RNAs involved in the proliferation of hepatocellular carcinoma: from basic research to clinical application
Department/ Laboratory : Gene therapy department, Center for Applied Medical Research (CIMA)
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Summary

Hepatocellular carcinoma (HCC) is the third cause of cancer-related death in the world. New therapies that increase patient survival are an urgent medical need. We believe that successful therapies for HCC could be based on non-coding genes. In spite of being the most numerous genes of the human genome, there are few studies with non-coding genes. The role of some of them in cell proliferation has been well-described, but they have not been used as therapeutic targets and their role in HCC is for the most part, unknown.

We have identified 13 long noncoding RNAs (lncRNAs) upregulated in HCC (15-10000 fold), as validated in two independent cohorts of human HCC. We now want to perform bioinformatic analyses that integrate patients' clinical, pathophysiological and genetic information with the expression of these lncRNAs, with the aim of finding significant associations with HCC drivers or with parameters of clinical relevance, prognosis, or response to treatment. When these associations are found, the expression levels of the selected lncRNAs will be validated in independent samples of human HCC with well-characterized clinical and genetic data and their potential as biomarkers will be evaluated.

Further, to assess the translational capacity of selected lncRNAs overexpressed in HCC, lncRNA-inhibition studies will be carried out using antisense oligonucleotides (ASOs) or genome editing technologies with CRISPR-Cas. After inhibition, we will study cell proliferation, cell cycle, apoptosis and senescence. The molecular mechanisms of those lncRNAs that impact cell growth will be addressed by whole-genome transcritome analysis. Our ultimate goal is the clinical development of the ASOs for the treatment of patients with HCC.

References

Iyer MK et al. The landscape of long noncoding RNAs in the human transcriptome. Nat Genet; 47: 199-208. 2015.

Schulze y cols., Exome sequencing of HCC identifies new mutational signatures and potential

therapeutic targets. Nat Genet. 47: 505-11. 2015.

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