Research Project Proposal
Academic year 2021-2022
Máster en Investigación Biomédica

Project Nº 44

Title: Role of KLF transcription factors in the pathogenesis of non-alcoholic fatty liver disease pathogenesis and liver cancer.

Department/ Laboratory
Liver Diseases Group
Department of Liver and Gastrointestinal Diseases
Biodonostia Health Research Institute (Donostia University Hospital)
Paseo del Dr. Begiristain s/n
20014 Donostia - San Sebastian

Director 1: Dr. Jesús María Bañales
Contact: jesus.banales@biodonostia.org/ jmbanales@unav.es
Tel: +34 943006067 (Office)
Codirector: Dr. Pedro Miguel Rodrigues
Contact: pedro.rodrigues@biodonostia.org
Tel: +34 943006067 (Office)

Summary: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the Western world, encompassing a wide spectrum of hepatic lesions. While simple steatosis constitutes the earliest and less severe stage, being relatively benign, progression towards non-alcoholic steatohepatitis (NASH) greatly increases the susceptibility to development of cirrhosis and hepatocellular carcinoma (HCC). Currently, the only therapeutic options with curative potential are surgical resection of the tumor and liver transplantation. Therefore, new therapeutic approaches are urgently needed to avoid disease progression and to treat patients, increasing their prognosis. Krüppel-like factors (KLFs) comprise a family of 17 transcription factors that significantly participate in several pathophysiological human processes. KLFs are key regulators of tissue homeostasis, organogenesis and cell differentiation but also strongly participate in cell metabolism and carcinogenesis. Still, the involvement of KLF members in the pathogenesis of NAFLD remains almost unknown.

Aims:

1) Evaluate the expression (mRNA and protein) of KLF members in distinct murine models of NAFLD and NAFLD-associated HCC.
2) Evaluate the levels of the most promising KLFs in samples from obese patients with NAFLD.
3) Investigate the effect of the most promising KLFs in modulating metabolism, inflammatory responses and cell death in *in vitro* models of NAFLD.

Methodology:

1) Expression of KLF members will be evaluated by qPCR, WB and IHQ.
2) Expression of selected KLFs will be evaluated in human samples by IHQ.
3) Cell death will be monitored by flow cytometry (PI-Annexin V staining). In parallel, cell death, metabolism and inflammatory markers will be evaluated by qPCR.

yes	
no	**X**

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?