Universidad de Navarra

MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2023-2024

Project Nº 43

Title: ***Role of the scavenger receptor MARCO in the progression of chronic liver disease and hepatocarcinogenesis: new diagnostic, prognostic and therapeutic strategy***

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Summary

Chronic liver diseases include a heterogeneous group of disorders characterized by progressive inflammation, injury and fibrosis, which can progress to cirrhosis and to the development of hepatocellular carcinoma (HCC). These patients frequently show increased intestinal permeability, favoring the translocation of bacterial components from the intestine to the liver. Innate immune cells recognize pathogens through pattern recognition receptors (PRRs), which include scavenger receptors (SRs) predominantly localized on macrophages and dendritic cells. The scavenger receptor MARCO is expressed on certain subsets of macrophages, and its expression can be induced after bacterial infection. MARCO seems to play a role in inflammatory responses and the clearance of pathogens. Therefore, we hypothesize that MARCO could play a key role in the progression of chronic liver disease.

Aims:

1. Analysis of MARCO expression in cirrhotic, HCC and normal human liver tissue and correlation with clinicopathological features.
2. Determination of the hepatic expression of MARCO in animal models of chronic liver injury, as well as in mouse primary liver cells *in vitro*.
3. Characterization of the role of MARCO modulating the hepatic inflammatory response.

Methodology:

1. MARCO hepatic expression (qPCR, WB, IHC) in cirrhotic, HCC and normal individuals, as well as in acute (CCl4) and chronic (CCl4, BDL, DEN, TAA) animal models of liver injury.
2. Primary liver cells (hepatocytes, cholangiocytes, Kupffer cells and hepatic stellate cells) will be characterized (qPCR, WB).
3. Chronic CCl4, BDL and TAA injury models in WT and *Marco*$^{-/-}$ mice: study of the liver phenotype (inflammation, fibrosis and carcinogenesis by qPCR, WB and IHC).

yes	
no	x

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