



### Research Project Proposal

Academic year 2019-2020

**Project Nº 18**

**Title:** *Role of the scavenger receptor MARCO in liver cancer: new diagnostic, prognostic and therapeutic strategy*

**Department/ Laboratory**

Liver Diseases Group,  
Department of Hepatology and Gastroenterology  
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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 primary liver tumors such as hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA). 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 in different cancers is associated with poor prognosis. Therefore, we hypothesize that MARCO could play a key role in primary liver cancer.

**Aims:**

1. Analysis of MARCO expression in cirrhotic, HCC, CCA and normal human liver tissue and correlation with clinicopathological features.
2. Determination of MARCO hepatic expression in mouse models of liver cancer, as well as in mouse primary liver cells *in vitro*.
3. Characterization of the role of MARCO in liver carcinogenesis.

**Methodology:**

1. MARCO hepatic expression (qPCR, WB, IHC) in cirrhotic, HCC, CCA and normal individuals, as well as in animal models of liver cancer (DEN, TAA and oncogene-driven HCC and CCA).
2. Primary liver cells (hepatocytes, cholangiocytes, Kupffer cells and hepatic stellate cells) will be characterized (qPCR, WB).
3. Experimental HCC and CCA model in Wt and *Marco*<sup>-/-</sup> mice: study of the carcinogenic role of MARCO *in vivo* analyzing tumor number and carcinogenic effects of MARCO in the liver in terms of inflammation, proliferation and injury by qPCR, WB and IHC.

yes	X	<b>Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?</b>
no		