Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 48* ASIGNADO

Title: Role of TREM2 receptor in acute and chronic liver injury

Department / Laboratory:
Liver Diseases Group,
Biodonostia Health Research Institute
Donostia University Hospital
Paseo del Dr. Begiristain s/n
20014 Donostia - San Sebastián

Director 1: Dra. María Jesús Perugorria

Contact:

E-mail: matxus.perugorria@biodonostia.org
Tel: +34 696018234 (Mobile) / +34 943006125 (Office)

Codirector: Dr. Jesús María Bañales

Contact:
E-mail: jesus.banales@biodonostia.org
Tel: +34 627401179 (Mobile) / +34 943006067 (Office)

Summary

Most chronic liver diseases develop inflammation and fibrosis overtime, which can progress to cirrhosis and to the development of hepatocellular carcinoma. Recently, it has been reported that such diseases have an increased intestinal permeability, favoring the translocation of bacterial components from the intestine to the liver; those components interact with toll-like receptors (TLRs) present in Kupffer Cells, (KC; ie. liver-resident macrophages) and in hepatic stellate cells (HSC; ie. fibrogenic cells). TLR signaling plays a key role in the development of liver inflammation, fibrosis and hepatocarcinogenesis. Recently, the TREM (triggering receptor expressed by myeloid cells) receptors have been discovered, which are believed to regulate the innate immune response through the modulation of TLR-mediated signaling. In particular, TREM-2 has recently been shown to be expressed on KCs and has been proposed to attenuate TLR4-mediated inflammation. We hypothesize that TREM-2 could play a key role in liver injury and inflammation.

Aims:

Analyze the expression of TREM-2 in human samples of normal and cirrhotic human livers of different etiologies, as well as in animal models of acute and chronic liver injury.

1. Characterize the role of TREM2 modulating the inflammatory response of the liver in an animal model of acute liver injury.
2. Elucidate the function of TREM-2 regulating inflammation in non-parenchymal hepatic cells.

Methodology:

1. Animal models of acute liver injury (WT and TREM-2KO mice)
2. Primary culture of non-parenchymal hepatic cells (KCs and HSCs).
3. mRNA expression analysis by RT-PCR and qPCR.
4. Protein detection by Western Blotting, ELISA and Immunohistochemistry.
5.

POSSIBILITY OF PhD

YES*

* (PhD grant required)