Research Project Proposal
Academic year 2020-2021

Máster en Investigación Biomédica

Project Nº 11

Title: ***Role of miR-506 in the regulation of the liver- and immunophenotype in primary biliary cholangitis***

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 943006125 (Office)

Summary Primary biliary cholangitis (PBC) is a chronic cholestatic liver disease associated with autoimmune phenomena targeting the intrahepatic bile duct cells, termed cholangiocytes. The aetiology of PBC is unknown and its pathogenesis remains obscure. Ursodeoxycholic acid (UDCA), an endogenous hepatoprotective and cholesteric bile acid, is the first line treatment that improves prognosis in 2/3 of patients. We have previously shown that miR-506 is specifically upregulated in cholangiocytes of patients with PBC, promoting cholestasis, autoimmunity and cell death [*Hepatology* 2012; *J Biol Chem.* 2015; *Hepatology* 2018; *J Hepatol* 2018]. Therefore, miR-506 arises as a key player in the promotion of PBC and as a new target for therapy. However, the mechanisms behind the immune regulation mediated by miR-506-overexpressing cholangiocytes remains unknown.

Aims:

1) Evaluate the expression of co-activator/co-inhibitory molecules and apoptosis-related genes in miR-506-overexpressing cholangiocytes.
2) Investigate the effect of miR-506-overexpressing cholangiocytes in macrophage polarization, Treg induction, Th cell profiles characterization and in B cell differentiation/proliferation.
3) Investigate the effect of immune cells in triggering cell death of miR-506-overexpressing cholangiocytes.
4) Evaluate miR-506 levels in the serum of patients with PBC and correlate its expression with clinicopathological features, patient´s outcome and response to therapy (UDCA).

Methodology:

1) Expression profile of miR-506-overexpressing cholangiocytes will be evaluated by qPCR and WB.
2) The phenotype of immune cells will be characterized by flow cytometry.
3) Cell death will be monitored by flow cytometry (PI-Annexin V staining) and confirmed WB and chemoluminescence.
4) Levels of miR-506 will be analyzed by qPCR after isolating serum miRNAs from patients with PBC.

yes	
no	**X**

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