

Research Project Proposal
Academic year 2016-2017

Project Nº 25
Title: Characterization of new hepatoprotective chimeric proteins based on fibroblast growth factor 19 (FGF19) and amphiregulin (AR) as therapeutic tools for the treatment of acute liver failure.
Department/ Laboratory Department of Hepatology/Matías Ávila's laboratory (CIMA)
Director 1 Iker Uriarte Díaz-Varela Contact: iuriarte@unav.es
<p>Summary Currently there are no pharmacological strategies able to preserve the viability of the hepatic parenchyma and to foster liver regeneration. This lack of therapeutic resources becomes apparent in different clinical situations such as liver resection of primary and secondary tumors, living donor liver transplantation, or acute liver failure induced by toxins, viruses or alcohol, conditions that are aggravated in the fatty liver. Fibroblast growth factor 19 (FGF19) and amphiregulin (AR) are among the most important proteins with hepatoprotective and pro-regenerative roles. Previously, we have developed two new chimeric proteins by fusing human Apolipoprotein A-I (ApoA-I) to FGF19 and AR, named Fibapo and Arapo respectively. This modification increases FGF19's and AR's hepatotropism and increases their half-life. The main goal of the project will be to test the therapeutic potential of these proteins in clinically relevant experimental models of acute liver injury and regeneration. Thus, the candidate will work with genetically modified mouse strains and hepatic cell lines. Routine laboratory technics will comprise real time PCRs, western blotting, ELISA, and immunohistochemistry, among others.</p> <p>References</p> <ol style="list-style-type: none"> 1. Sarin SK, Choudhury A. Acute-on-chronic liver failure: terminology, mechanisms and management. <i>Nat Rev Gastroenterol Hepatol.</i> 2016 Mar;13(3):131-49. 2. Uriarte I, Fernandez-Barrena MG, Monte MJ, et al. Identification of fibroblast growth factor 15 as a novel mediator of liver regeneration and its application in the prevention of post-resection liver failure in mice. <i>Gut.</i> 2013 Jun;62(6):899-910. 3. Berasain C, Avila MA. Amphiregulin. <i>Semin Cell Dev Biol.</i> 2014 Apr;28:31-41.



POSSIBILITY OF PhD

YES ** (PhD grant required)