Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 2

Title: Role of amphiregulin in liver metabolism

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Summary

Amphiregulin (AR) is a soluble growth factor synthesized as a transmembrane precursor that binds the epidermal growth factor receptor (EGFR). During the last decade our group has characterized the role of AR in liver pathophysiology (reviewed in Berasain & Avila 2014). We have demonstrated that AR is not expressed in the normal liver but is induced very quickly after damage to perform hepatoprotective and regenerative roles. AR expression is induced in the liver of cirrhotic patients and in the hepatocarcinomas (HCC) and our data demonstrate that the sustained induction of AR during chronic damage can participate in the development of liver fibrosis and in the malignant transformation of the hepatocytes (Perugorria et al. and Castillo et al).

Obesity and metabolic syndrome are at the origin of the non-alcoholic fatty liver disease (NAFLD), actually the main etiologic cause of liver cirrhosis and HCC. Our preliminary data demonstrate that AR expression is induced in the liver of NAFLD patients and in the liver of obese mice (ob/ob).

In the present project we will take advantage of all the in vitro tools developed in our laboratory, and of different diet and metabolic models applied to the colonies of AR knockout mice (KOAR) and liver-specific AR transgenic mice (TgAR) to characterize the role of AR in liver metabolism and the potential of AR-expression manipulation in the progression of NAFLD.

References:

- Berasain C, Avila MA. “Amphiregulin” . Semin Cell Dev Biol. 2014 Apr;28:31-41. doi:10.1016/j.semcdb.2014.01.005. IF: 6.2

- Perugorria MJ, Latasa MU, Nicou A, Cartagena-Lirola H, Castillo J, Goñi S, Vespasiani-Gentilucci U, Zagami MG, Lotersztajn S, Prieto J, Avila MA, Berasain C. “The epidermal growth factor receptor ligand amphiregulin participates in the development of mouse liver fibrosis”.Hepatology. 2008 Oct; 48(4):1251-61. IF: 11.09

- Castillo J, Goñi S, Latasa MU, Perugorría MJ, Calvo A, Muntané J, Bioulac-Sage P, Balabaud C, Prieto J, Avila MA, Berasain C. "Amphiregulin induces the alternative splicing of p73 into its oncogenic isoform DeltaEx2p73 in human hepatocellular tumours".Gastroenterology. 2009; 137(5):1805-15. IF: 12.8

POSSIBILITY OF PhD

YES*

* (depending on the possibility of obtaining a PhD grant)