

Research Project Proposal
Academic year 2016-2017

Project Nº 37 ASIGNADO
<p>Title: Role of endothelins in the pathophysiology of polycystic liver diseases (PLDs)</p>
<p>Department/ Laboratory Liver Diseases Group, Department of Gastrointestinal and Liver Diseases. Biodonostia Health Research Institute (Donostia University Hospital), San Sebastian.</p>
<p>Director Dr. Jesús María Bañales Asurmendi Contact: jesus.banales@biodonostia.org</p> <p>Codirector: Dra. María Jesús Perugorria Montiel Contact: matxus.perugorria@biodonosti.org</p>
<p>Summary</p> <p>Polycystic liver diseases (PLDs) are genetic disorders characterized by biliary cystogenesis, which is main cause of morbidity. Cyst growth is the result of increased proliferation, secretion and matrix-metalloprotease activity in bile duct epithelial cells (i.e. cholangiocytes). Current therapeutic options show short-term and modest beneficial effects. So, the understanding of the molecular mechanisms involved in the development and progression of PLDs is key in order to find new potential targets for therapy.</p> <p>Increasing evidence indicates that endothelins (i.e., ET-1 and ET-3) promote proliferation and secretion in several cell types and tissues, and are important in the pathogenesis of diseases such as hypertension, atherosclerosis, heart failure and renal failure. Here, we hypothesize that endothelins might promote biliary cystogenesis by stimulating the proliferation and secretion of cholangiocytes.</p> <p>We propose the following aims of study:</p> <ol style="list-style-type: none"> 1. Expression of endothelins and its receptors in both normal and cystic human cholangiocytes in culture. 2. Determination of the presence (and levels) of endothelins in human hepatic cystic fluid and normal human bile. 3. Role of endothelins on the proliferation of normal and polycystic human



cholangiocytes and molecular mechanisms of action.

Methodology:

- 1-** Primary culture of normal and polycystic human cholangiocytes.
- 2-** Gene expression: real-time quantitative polymerase chain reaction (qPCR) and western blotting.
- 3-** Endothelins elisa kit.
- 4-** Proliferation assays: Flow Cytometry.

POSSIBILITY OF PhD

YES *

* (PhD grant required)