

Research Project Proposal
Academic year 2015-2016

| |
|---|
| Project Nº 6 |
| Title: Role of the splicing factor Slu7 in liver pathophysiology |
| Department/ Laboratory Laboratory 4.02. Division of Hepatology. CIMA |
| Director: Carmen Berasain Contact: cberasain@unav.es 948 194700 Ext 4020 |
| Codirector: Raquel Urtasun Contact: rurtasun@unav.es 948 194700 Ext 4021 |
| <p>Summary</p> <p>Results from our laboratory (Castillo et al. 2009) show that the expression of the splicing factor Slu7 is downregulated in the cirrhotic liver and in hepatocellular carcinoma (HCC). We have demonstrated that this expression is controlled by the growth factor amphiregulin (AR), a member of the epidermal growth factor family, which plays multiple relevant roles in liver pathology (Berasain et al. 2014). More recent results suggest that the observed hepatic SLU7-downregulation in chronic liver patients can be responsible for the loss of hepatic functions observed in those patients, as we have demonstrate that SLU7 exerts an essential role in the liver, maintaining the phenotypic characteristics of the adult liver and controlling multiple metabolic functions and hepatic quiescence (Elizalde et al. 2014). Our unpublished data also demonstrate that SLU7 has a role in the survival of HCC cells (Urtasun et al. manuscript in preparation). SLU7 performs all these functions through the regulation of the expression and the alternative splicing of multiple genes. The actual aim of our laboratory is to better characterize the role of SLU7 in liver pathophysiology and to delineate the mechanisms implicated in both the regulation of SLU7 expression and its activity. To this end we will perform loss of function experiments in vitro (siRNAs) in HCC cells and in vivo (AAV-shRNAs) in mice and we will also characterize a newly developed conditional SLU7-knockout mouse.</p> <p>References</p> <p>- 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</p> |



tumours". Gastroenterology. 2009;137(5):1805-15. IF: 12.8

- 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

- Elizalde M, Urtasun R, Azkona M, Latasa MU, Goñi S, García-Irigoyen O, Uriarte I,
Segura V, Collantes M, Di Scala M, Lujambio A, Prieto J, Ávila MA, Berasain C. "Splicing
regulator SLU7 is essential for maintaining liver homeostasis". J Clin Invest 2014 Jul
1;124(7):2909-20. IF: 13.76

POSSIBILITY OF PhD

YES*

* (PhD grant required)