



## Research Project Proposal

Academic year 2018-2019

### Project Nº 2

**Title:** *Role of SLU7 controlling splicing and DNA methylation in cancer*

**Department/ Laboratory.** *Program of Hepatology (Laboratory 4.02). CIMA.*

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**Summary** Our laboratory has demonstrated that the splicing factor SLU7 is essential to maintain the differentiated/functional phenotype of the liver (Elizalde et al. J. Clin. Invest. 2014). We also found that SLU7 expression is reduced in the damaged liver of cirrhotic patients and in HCC (Castillo et al. Gastroenterology 2009). Unexpectedly we have also demonstrated that SLU7 is essential for the survival of cancer cells from different origin (Urtasun et al. Oncogene 2016) being required for the progression through the cell cycle. Our more recent unpublished results show that SLU7 is necessary to maintain genome integrity and probably the activity of the non-sense mRNA mediated decay (NMD) system. Mechanistically we have identified multiple targets which alternative splicing and/or expression depend on SLU7.

In the present project we plan to better characterize these targets and the mechanisms implicated in the phenotypes already described. In addition, we want to study the possible implication of SLU7 in the regulation of DNA methylation.

To this aim, the methodology to be used will be:

- different human cancer cell lines,
- transfections with specific siRNAs,
- assays to measure cell proliferation, apoptosis, DNA methylation and NMD activity, among others,
- techniques such as Western blot, real time PCR, methylation specific PCR (MSP) and co-immunoprecipitation.

yes	
no	X

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