Research Project Proposal
Academic year 2019-2020

Project Nº 10

Title: Coupling epigenetics and RNA splicing in cancer

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

Director 1: Carmen Berasain
Contact: *cberasain@unav.es*
Codirector: María Arechederra
Contact: *macalderon@unav.es*

Summary Transcription is a highly dynamic and precisely controlled process that allows the expression of genes in a tissue and temporal specific manner. In cancer, transcriptional programs are dysregulated leading to tumour progression. Epigenetic modifications and splicing events serve as key regulatory process for gene expression before and after transcription, and both events are known to be altered in cancer.

We have recently demonstrated that the splicing factor 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 (Jimenez et al. NAR 2019). Our more recent unpublished results reveal that SLU7 is required to preserve DNA methylation, since depletion of SLU7 drastically reduced DNMT1 protein levels and global DNA methylation content. Importantly, we have found that SLU7 and DNMT1 interact in different cell lines, uncovering a new protein complex coupling epigenetics and RNA splicing.

In the present project, we plan to understand the mechanism by which SLU7 regulates DNMT1 levels and the biological relevance of the SLU7/DNMT1 protein complex. We also plan to explore whether other splicing factors such as SRSF1 and SRSF3 are implicated in the regulation of DNA methylation.

- Methodology to be used in the present proposal: cell culture (different human cancer cell lines, transfections with specific siRNAs, drug treatments), assays to measure cell proliferation, DNA methylation or apoptosis, among other, using different techniques such as Western blot, real time PCR, methylation specific PCR (MSP) or co-immunoprecipitation.

yes		**Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?**
no	X	