Máster en Investigación Biomédica

Project Nº 41
Title: A genome-wide approach to discover small circular RNAs under physiological and stress conditions.

Department/ Laboratory Laboratory 4.08: The Mechanism and Relevance of the Unfolded Protein Response in Neurodegeneration Laboratory of Department of Gene Therapy and Regulation of Gene Expression. CIMA.

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Summary

In the last years, circular RNAs (circRNAs) have emerged as a new type of RNA molecules that utilize unexplored mechanisms to participate in the participate in cell metabolism under a wide variety of physiological and pathological conditions. High throughput sequencing of circular RNAs revealed that most of them as produced by the nuclear spliceosome, often in a stress-dependent manner, but other biosynthetic mechanisms can also produce circRNA molecules. The central nervous system is the tissue where circRNAs are most abundant, and its dysregulation has been already observed in many pathologies.

In our group, we study the non-canonical splicing of XBP1 mRNA, that occurs in the cytosolic surface of the endoplasmic reticulum (ER) under ER stress conditions. This unique splicing reaction is catalysed by the ER stress sensor IRE1 which removes a short 26-nucleotide intron from the XBP1 mRNA, and the tRNA ligase RTCB, that ligates the resulting exons and circularizes this small intron. When we tried to detect this small circular RNA, we realized that conventional methods are hardly able to detect very small circRNA. The aim of this project is to identify the abundance and diversity of short circular RNAs in cell under normal and ER stress conditions, as well as in samples obtained from animal or neuronal models of amyotrophic lateral sclerosis, an ER stress-linked devastating neurodegenerative disorder.

By using two independent approaches, we will develop a protocol to isolate small circular RNA from these samples to then generate sequencing libraries that after deep sequencing will be analysed with customized bioinformatic tools.

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