Research Project Proposal
Academic year 2018-2019

Project Nº 42

Title: *Small RNAs and the Unfolded Protein Response: Development of a method to identify small circular RNAs.*

Department/ Laboratory Laboratory of Regulation of Gene Expression and Cellular Stress. Department of Gene Therapy and Regulation of Gene Expression, CIMA etc.

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Summary *Short summary of the project with a **maximum extension of 250 words**, including the goals and the methodology that will be used.*

In response to changes in the environment eukaryotic cells have developed different stress response mechanisms that enable the cells to adapt to such changes and maintain homeostasis. Among them, the unfolded protein response (UPR) is key to ensure that the folding of membrane and secreted proteins in the endoplasmic reticulum (ER) occurs properly. A key UPR mechanism conserved from yeast to human is the non-canonical splicing of a unique mRNA that encodes a transcription factor, XBP1 or HAC1 in human and yeast cells, respectively. Together with this unconventional splicing reaction, our unpublished data indicated that other cellular RNA processing events are also altered. In particular our initial RNA sequencing experiments have revealed that in cells under stress a variety of small linear and circular RNAs are produced. Due to their reduced size, the circular molecules present are really hard to detect when we use the current RNAseq approaches. To be able to explore the diversity of small, stress-induced circular RNAs and the role of UPR introns we propose to:

1) Develop a methodology to isolate and identify by deep sequencing small circular RNAs. We will setup a biochemical method to purify these RNA species and identify their sequence by high-throughput RNA sequencing and bioinformatic validation of RNA junction sites.
2) We will investigate the role of HAC1/XBP1 introns in the UPR. By using genetic approaches we will establish the regulatory role of these sequences in the response to stress.

yes	
no	**X**

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