Instituto de Biología Funcional y Genómica

Programa de Seminarios Externos "Dionisio Martín Zanca"

2023 - 2024

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Genomic dissection of gene expression: from co-translational mRNA decay to transcriptional memory and cellular plasticity

Viernes 12 Enero 2024

Hora: 12:00 pm
Lugar: Salón de actos del IBFG
Web: https://ibfg.usal-csic.es/semext.php
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Abstract

We have previously shown that during co-translational mRNA decay, 5'-3' exonucleases produce an in vivo toeprint of the position of the last (most 5') trailing ribosome. Thus, by sequencing the 5'P mRNA degradation intermediates naturally present in cells (5PSeq) we can measure the in vivo position of the last translating ribosome. I will discuss how the application of 5PSeq to complex microbial samples (metadegradome sequencing), provides a fast, species-specific post-transcriptional characterization of bacteria responses to drugs and environmental perturbations. Next, I will show how ribosomes can act a molecular sensor to modulate transcriptome abundance via generalized frameshift and out-of-frame mRNA decay. Combining the use of 5PSeq, ribosome profiling and mRNA metabolic labelling, our data shows how, in response to poor nutritional conditions, the bulk of the S. cerevisiae transcriptome (77% of the genome) undergo -1 ribosome frameshifts and experiences an accelerated out-of-frame co-translational mRNA decay. I will further discuss how low codon optimality is a key factor in this process and provide evidence of its conservation from bacteria to humans. We hypothesize that this is a new mechanism providing direct regulatory feedback coupling protein demand with the control of mRNA abundance. Next, I will describe our effors on transcriptional memory and cancer cellular plasticity. I will explain our work combining genomics with CRISPR-KO screens to identify novel factors controlling cellular plasticity in Chronic Myeloid Leukaemia. Finally, I will present our recent work in GEMLI (Gene Expression Memory-based Lineage Inference), a computational tool allowing to determine cell lineages solely from scRNA-seq datasets without the need of genetic barcodes.

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