

Instituto de Biología Funcional y Genómica

Programa de Seminarios Externos

"Dionisio Martín Zanca"

2023 - 2024

María Vera

*Department of Biochemistry, McGill University, Montreal
Canada*

***Imaging single mRNAs uncovers
new mechanisms to sustain
neuronal proteostasis***

Viernes **22** *Diciembre*
2023

Hora: 12:30 pm

Lugar: Salón de actos del IBFG

Web: <https://ibfg.usal-csic.es/semext.php>

Contacto: Olga Calvo (ocalvo@usal.es)

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Abstract

In this seminar, I will present our ongoing research in the regulation of expression of Heat Shock Proteins (HSPs) in neurons undergoing pathophysiological stresses and their relation to age-related neurodegenerative diseases. HSPs are molecular chaperones in charge of protein folding and homeostasis. Cells have the remarkable capacity to tailor the expression of HSPs to the extent of protein damage. The precise regulation of HSP expression is required to safeguard protein homeostasis and ensure cell functionality upon proteotoxic damage. Using single-molecule fluorescence microscopy techniques, we have discovered that beyond the activation of HSP transcription, neurons regulate the subcellular distribution of HSP mRNAs in response to stress. mRNA localization to neuronal projections and the local regulation of their translation emerges as a novel mechanism to regulate the local pool of HSPs and sustain proteostasis at neuronal processes. Beyond uncovering fundamental aspects of neuronal proteostasis, our findings have critical implications for neurodegenerative diseases. We identified two amyotrophic lateral sclerosis-related proteins, fused in sarcoma and heterogeneous nuclear ribonucleoprotein A2/B1, that guide the localization of constitutive HSP mRNAs to the dendrites. Dendritic attrition and loss of synaptogenesis are common signs of diverse neurodegenerative diseases, and defects in dendritic HSP mRNA localization offer a molecular explanation for these events. As I share our advancements on this project, I will introduce several mRNA imaging technologies that are helping us to answer fundamental gene expression regulation questions.