Title:
Calcium-driven protein redistribution: a new paradigm for nuclear integration during stress

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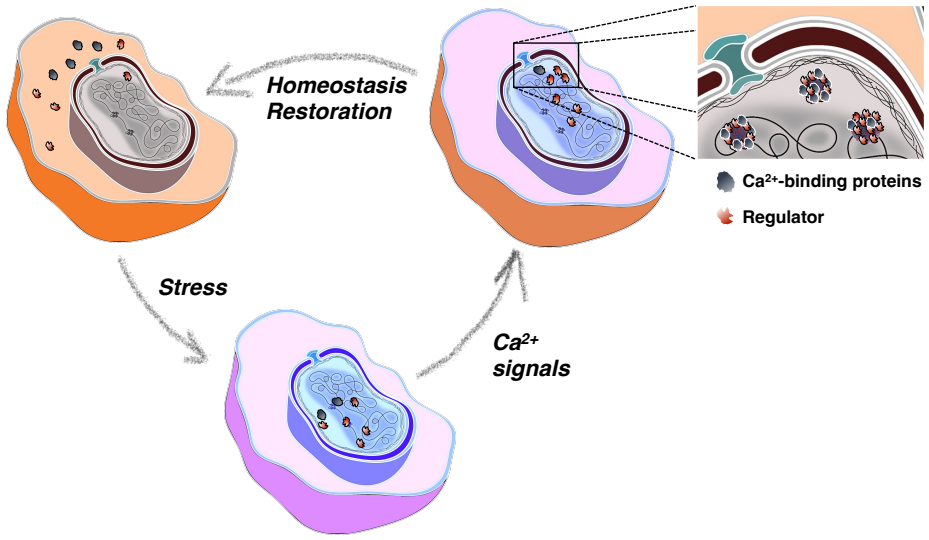
Research Theme / Topic: Nuclear integration during stress

It is hardly necessary to point to the centrality of the nucleus in every cellular event. Within this compartment is stored the canvas containing the information necessary for the constitution of all cellular components (with the notable exception of those produced by the mitochondrial DNA). Even more importantly, the nucleus can respond to the cellular needs with remarkable plasticity. Interestingly, the regulatory pathways coordinating the functional integration of the nucleus are not fully understood. Since first observed under a microscope, the nuclear milieu appears inhomogeneous and is characterized by several structures based on proteins and nucleic acids called membraneless organelles (nucleolus, PML bodies etc.) that contribute to the compartmentalization of the nucleus an offer optimal environment for specific reactions to occur[1]. A key characteristic of these structures is their dynamic nature and stress-responsiveness, however the upstream signaling pathways and components involved in this process remain largely undefined[2].
The proposed projects aims to understand whether and how the prototypical second messenger Calcium is involved in nuclear compartmentalization through membraneless organelles. The candidate will develop a comprehensive multi-disciplinary approach starting from bioinformatic-based identification of Ca^{2+}-binding proteins able to enter the nucleus and capable of forming or participating to membraneless organelles. The behavior of putative targets in response to Ca^{2+} will be testing using live cell imaging, while their involvement to known membraneless organelles will be followed by immunofluorescence. Changes in composition of specific membraneless organelles in response to Ca^{2+} will be assessed by proximity labelling using biotinylases[3] (TurboID, APEX2) coupled to mass spectrometry, while the functional outcomes will be assessed by total RNA sequencing. This project will be performed mainly in Pavia, however several national and international collaborations are already in place.



References:

1. Gomes E, Shorter J. The molecular language of membraneless organelles. *J Biol Chem*. 2019;294(18):7115-7127. doi:10.1074/jbc.TM118.001192
2. Iannucci LF, D'Erchia AM, Picardi E, et al. Cyclic AMP induces reversible EPAC1 condensates that regulate histone transcription. *Nat Commun*. 2023;14(1):5521. doi:10.1038/s41467-023-41088-x
3. Branon TC, Bosch JA, Sanchez AD, et al. Efficient proximity labeling in living cells and organisms with TurboID. *Nat Biotechnol*. 2018;36(9):880-887. doi:10.1038/nbt.4201