PhD position

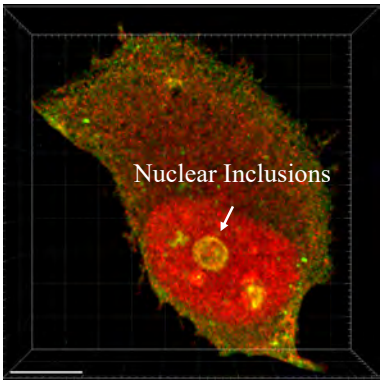
CRBM-CNRS-Montpellier

The role of Ubiquitin and Ubiquitin-like molecules in the nuclear Protein Quality Control system

Project background:

Organisms are constantly exposed to environmental stresses that cause protein damage (proteotoxic stress). A series of sophisticated mechanisms that constitute the so-called Protein Quality Control (PQC) system ensure the detection, repair and/or elimination of protein damage in order to maintain protein homeostasis (proteostasis). Unattended damaged proteins tend to form aberrant protein inclusions either in the cytoplasm or in the nucleus and are linked to many neurodegenerative diseases (Alzheimer's disease, Parkinson's disease), cancer and aging.

The family of Ubiquitin and Ubiquitin-like molecules (Ubls) such as SUMO and NEDD8, plays a critical role in all aspects of the PQC system. Tagging of misfolded proteins with Ubiquitin chains is the key step towards the elimination of aggregation prone proteins and aberrant inclusions.



Aim of the project:

To reveal fundamental elements for the control of the PQC system in the nucleus. In particular, to determine the role of Ubiquitin/Ubls in the elimination of nuclear protein inclusions and the impact on cell survival. The candidate will be involved in a multidisciplinary collaborative project between CRBM (Montpellier), CBI and IPBS (Toulouse) that combines molecular biology/biochemistry, state of the art live-imaging and mass spectrometry-based proteomics, using mammalian cells, *C. elegans* and mouse-derived neurons.

Start date: September/October 2022

Applications in the form of a CV and cover letter, including the names and addresses of 2 referees, should be sent to **Dr Dimitris Xirodimas**, dimitris.xirodimas@crbm.cnrs.fr https://www.crbm.cnrs.fr/dimitris-xirodimas/?lang=en,

Selected references

1. Meszka et al. (2022). Mixed in chains: NEDD8 polymers in the Protein Quality Control system. *Semin Cell Dev Biol*. S1084-9521(22)00013-1. doi: 10.1016/j.semcdb.2022.01.005.
2. Lobato GS, et al. (2021). Proteome-wide identification of NEDD8 sites reveals distinct proteomes for canonical and atypical NEDDylation. *Cell Reports,* 34(3):108635. doi: 10.1016/j.celrep.2020.108635.
3. Bailly AP, et al. (2019). The balance between mono and NEDD8-chains controlled by NEDP1 upon DNA damage is a regulatory module of the HSP70 ATPase activity. *Cell Reports* 29, 212–224.
4. Maghames C, et al. (2018). NEDDylation promotes nuclear protein aggregation and protects the Ubiquitin Proteasome System upon proteotoxic stress. *Nat. Commun.* 9:4376 | DOI: 10.1038/s41467-018-06365-0.

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