Master 2 internship project
Year 2019-2020

Laboratory/Institute: Institut de Biologie Structurale **Director:** W. Weissenhorn
Team: ELMA **Head of the team:** B. Franzetti

Name and status of the scientist in charge of the project: B. Franzetti **HDR: yes** X **no** ☐
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Program of the Master's degree in Biology:

☐ Immunology, Microbiology, Infectious Diseases X Integrative Structural Biology
☐ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology
☐ Planta International

Title of the project:

Characterization of a molecular networks triggering the coordination of protein and RNA destruction machines in Archaeal cells.

Objectives :

The objective is to highlight for the first time the role of a protein in the coordination of the proteasome with RNA modification machineries, with a view to promoting a recycling of defective ribosomes in hyperthermophilic archaea.

Abstract:

The proteasome is a cellular complex responsible for the destruction of defective proteins in the cytoplasm. Proteasome regulation is a key function in aging processes and in adapting to environmental stress. To unravel unknown proteasome regulatory pathways, we used an Archean homologue of the eukaryotic proteasome as "bait" in interactomics studies. We identified one uncharacterized protein, PBP11, interacting directly with the proteasome regulatory particle. Interestingly, the structure and interaction properties of PBP11 also revealed an association with RNA quality control systems. The effect of PBP11 and its partners on the proteasome degradation activity will be studied *in vitro* using model substrates and purified ribosomes. In vitro reconstructed complexes involving PBP11 or complexes captured *in vivo* from *P. abysii* or genetically modified *T. barophilus* cells using various affinity approaches (coll IFREMER-Brest) will be characterized at IBS using an integrated structural biology study with a focus on cryo-electron microscopy approaches. The project is part of an ANR research program (period covered: 2019-2022).

Methods :

Recombinant protein purifications, native affinity purifications, biophysical characterizations (Sec-MALS, AUC, SAXS), Protein degradation assays pull down, X-ray crystallography; cryo-Electron Microscopy.

Up to 3 relevant publications of the team:

1. 1
. Cao, S., S. Engilberge, E. Girard, F. Gabel, B. Franzetti & J.A. Maupin-Furlow, (2017) Structural Insight into Ubiquitin-Like Protein Recognition and Oligomeric States of JAMM/MPN+ Proteases. Structure.
2. 2
. Ibrahim, Z., A. Martel, M. Moulin, H.S. Kim, M. Hartlein, B. Franzetti & F. Gabel, (2017) Time-resolved neutron scattering provides new insight into protein substrate processing by a AAA+ unfoldase. Scientific reports 7: 40948.
3. 3
. Colombo, M., Girard, E., and Franzetti, B. (2016) Tuned by metals: the TET peptidase activity is controlled by 3 metal binding sites. Scientific reports 6, 20876

Requested domains of expertise :

Structural Biology; Cellular Biochemistry.