Master 2 internship project
Year 2020-2021

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 novel ribosome quality control system in extremophiles

Objectives :

The objective is to unravel the role of a newly identified protein network in the recruitment of the proteasome machinery toward ribosomes with a view to promoting the destruction of defective translational products in extreme environmental conditions.

Abstract:

The proteasome is a cellular complex responsible for the destruction of defective proteins in the cytoplasm. To unravel unknown proteasome regulatory pathways and to understand how extremophilic microorganisms adapt to hostile environments such as the deep sea hydrothermal vents, we used an Archean proteasome as "bait" in interactomics studies. We identified several uncharacterized protein interacting directly with the proteasome regulatory particle. Interestingly, the structure and interaction properties of a small partner called PBP11 also revealed an association with the ribosome and 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: 2019-2023).

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. . 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. 1
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. 2
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 3

Requested domains of expertise :

Integrative Structural Biology; Biochemistry.