Internship project Master 2
Year 2017-2018

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 the Master's degree in Biology:

☐ Neurosciences and Neurobiology ☐ Immunology, Microbiology, Infectious Diseases

X Integrative Structural Biology ☐ Physiology, Epigenetics, Development, Differentiation

Title of the project: "Characterization of a novel proteasome regulator"

Objectives (up to 3 lines):

The project aims at determining the function and mode of action of a newly identified proteasome interacting factor.

Abstract (up to 10 lines):

The 26S proteasome is a cellular machine responsible for the specific degradation of ubiquitinated proteins substrates. Its activity is tuned by several types of regulatory complexes representing important targets in biomedecine, in particular in cancer diseases. The detailed composition of these regulatory particles remains partially understood due to the intrinsic instability of the holocomplexes in vivo. The Master project aims at determining the function and mode of action of a newly identified proteasome regulatory factor, called ZY3, that we recently discovered in extremophilic archaea using interactomics approaches. Recombinant variants of the ZY3 protein have been produced and the atomic structure of the protein was determined by X-ray crystallography. Its interaction with proteasome subunits will be studied using a range of biophysical methods such as SPR, AUC, SecMALs etc. The conformational changes associated with ZY3 binding will be studied by SAXS and X-ray crystallography. Functional. In vitro functional assays will be performed to unravel the effect of ZY3 on proteasome unfoldase and proteolytic activities.

Methods (up to 3 lines):

Unfoldase and protein degradation assays; X-ray crystallography; Small Angle X-ray Scattering (SAXS); analytical ultracentrifugation (AUC); Surface plasmon resonance (SPR).

Up to 3 relevant publications of the team:

• 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.

• 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.

• Cao, S., Engilberge, S., Girard, E., Gabel, F., Franzetti, B & Maupin-Furlow, JA. (2017) Structural insight into ubiquitin and ubiquitin-like protein recognition and oligomeric states of JAMM/MPN+ proteases. **Structure**. In press

Requested domains of expertise (up to 5 keywords):

Biochemistry, Integrative Structural Biology