Grenoble Alliance for Integrated Structural & Cell Biology

GRAL MASTER 2 RESEARCH SCHOLARSHIP - Program 2017 - 2018

INTERNSHIP PROPOSAL

Institute and Group: IBS, group ELMA
Supervisor: Bruno Franzetti
Phone: +33 (0)4 57 42 85 69
Email:franzetti@ibs.fr

Title: Characterization of novel proteasome regulatory systems

5 Keywords: ATP-dependent protease, large molecular assemblies, X-ray crystallography, Small angle scattering, Cryo-EM.

Description of the project: The proteasome is a large molecular machine responsible for the maintenance of intracellular protein homeostasis and the regulation of specific cellular functions. A defective proteasome function is associated with ageing and proteasome inhibitors are anticancer drugs. Using in vivo pull down experiments in model archaeal cells we recently identified 3 novel proteasome interacting proteins, including a putative peptidase. These proteins may represent interesting targets in biomedicine and biotechnologies. To unravel their role in the regulation of the proteasome function, we take a multidisciplinary approach combining biochemical experiments with modern structural biology techniques. The student will contribute to characterize the association of the novel proteins with the proteasome regulatory AAA-ATPase complex, to assess for their effect on the proteasome function and to determine their atomic structure alone and in complex with their respective proteasome subunit partners using advanced crystallography, small angle scattering and cryo-EM single particle analysis.

Relevant publications of the team:

1. Colombo M, Girard E, Franzetti B. (2016) Tuned by metals: the TET peptidase activity is controlled by 3 metal binding sites. ***Sci Rep.*** Feb 8; 6:20876.
2. Ibrahim, Z., Martel A., Moulin, M., Kim, H., Härtlein, M., Franzetti, B., and Gabel, F. Time-resolved neutron scattering provides new insight into protein substrate processing by a AAA+ unfoldase. ***Sci Rep****. In press*
3. Appolaire, A., M.A. Dura, M. Ferruit, J.P. Andrieu, A. Godfroy, S. Gribaldo & B. Franzetti, (2014) The TET2 and TET3 aminopeptidases from Pyrococcus horikoshii form a hetero-subunit peptidasome with enhanced peptide destruction properties. ***Mol Microbiol*** 94: 803-814.