Grenoble Alliance for Integrated Structural & Cell Biology

INTERNSHIP PROPOSAL

Institute and Group: Institut de Biologie Structurale / Extremophiles and Large Molecular Assemblies group (ELMA)

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Research project title: Characterization of a molecular core connecting the proteasome with RNA quality control machineries.

5 Keywords to describe the project: Proteasome regulation; native macromolecular assemblies; cryoEM; stress response.

Description of the project:

The proteasome system plays important roles in stress response and ageing by eliminating damaged molecular edifices. Extremophilic microorganisms use optimized quality control systems to cope with sharp environmental changes. In hyperthermophilic archaea (HA), we recently identified a small proteasome interacting protein of unknown function (PBP11). The PBP11 interaction network *in vivo* and its X-ray structure suggest that it acts as a critical nexus in coordinating the proteasome degradation activity and the RNA decay machineries to secure the quality of the ribosomal proteins. To verify this hypothesis, we want to determine the cryo-EM structures of native macromolecular edifices associating PRB11 with its proteasomal regulatory subunits partners. For this, native holo-complexes will be pulled out from HA cell using tagged PRB11. The complexes will also be reconstructed in vitro with recombinants proteins and studied using a range of biophysical methods such as SecMALs, AUC and SAXS. Functional biochemical assays will also be performed to unravel the effect of the Z3 complexes on proteasome unfoldase and proteolytic activities. Candidates should have a strong background in cellular biochemistry and be interested in integrative structural biology.

Justification that the internship's subject fits with the general theme of GRAL:
The project fits with the GRAL advanced Integrative structural biology theme with a focus on native complexes.

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