Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2023-2024

Laboratory/Institute: IBS (Institut de Biologie Structurale) **Director:** Winfried Weissenhorn
Team: NMR of large biomolecular assemblies **Head of the team:** Jérôme Boisbouvier

Name and status of the scientist in charge of the project: Jérôme Boisbouvier **HDR: yes**
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Program of the Master's degree in Biology:

☐ Microbiology, Infectious Diseases and Immunology X Structural Biology of Pathogens
☐ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology

Title of the project:

Structural and Functional investigation of ClpX/ClpP proteolytic machine in action

Objectives (up to 3 lines):

The aim of the project is to understand the mechanism of the ClpP/X machine, by obtaining detailed structural and kinetic information on the mechanisms of these ATP-driven proteolytic machines under functional conditions.

Abstract (up to 10 lines):

Caseinolytic proteases are large, barrel-shaped serine proteases found in bacteria. Although ClpPs are capable of degrading small peptides on their own, their association with ClpX, an unfoldase, is required to degrade larger peptides and proteins. ClpX is an energy-dependent AAA+ ATPase, capable of unfolding and translocating the client protein into the ClpP barrel pore. The ClpP/X assembly, a 0.8 MDa complex, plays an active role in the survival and virulence of pathogenic bacteria. The aim of the project is to gain a detailed understanding of the mechanism of the ClpP/X machine, i.e. to obtain information on the intermediate states and kinetics of the ClpP/X functional cycle in the presence of ATP and in interaction with the client protein. To achieve this goal, we will integrate state-of-the-art methods in high-field nuclear magnetic resonance spectroscopy and cryo-electron microscopy. This integrated structural biology project offers a unique opportunity to study, at atomic resolution, the mechanism of a dynamic molecular machine in the heat of action.

Methods (up to 3 lines):

Solution NMR spectroscopy combined with in-house developed cell-free production and isotope labeling methods will be used to observe this large machinery as it processes substrate proteins such as FtsZ. These results will be combined with cryoEM studies to obtain high-resolution structural models.

Up to 3 relevant publications of the team:

Visualizing the Transiently Populated Closed-State of Human HSP90 ATP Binding Domain
Henot, Rioual, Favier, Macek, Crublet, Josso, Brutscher, Frech, Gans, Loison, Boisbouvier
Nature Communications (2022). https://www.nature.com/articles/s41467-022-35399-8

Structural Basis for the Inhibition of IAPP Fibril Formation by the Co-Chaperonin Prefoldin
Torner, Kupreichyk, Gremer, Colas Debled, Fenel, Gans, Willbold, Schoehn, Hoyer, Boisbouvier.
Nature Communications (2022). https://www.nature.com/articles/s41467-022-30042-y

Structural Investigation of a Chaperonin in Action Reveals How Nucleotide Binding Regulates the Functional Cycle
Mas, Guan, Crublet, Colas Debled, Moriscot, Gans, Schoehn, Macek, Schanda, Boisbouvier
Science Advances (2018). https://www.science.org/doi/10.1126/sciadv.aau4196

Requested domains of expertise (up to 5 keywords): Biochemistry, Structural Biology