

**Internship project Master 2
Year 2017-2018**

Laboratory/Institute: Institut de Biologie Structurale
Team: Biomolecular NMR Spectroscopy

Director: Winfried Weissenhorn
Head of the team: Jerome Boisbouvier

Name and status of the scientist in charge of the project:

Jerome BOISBOUVIER / CNRS Research Director

HDR: YES

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Program the Master's degree in Biology:

Integrative Structural Biology

Title of the project: **Chaperonin Interactions with Amyloidogenic proteins**

Objectives: The main objective of this project is to understand how large hsp60 chaperonin/prefoldin machinery interacts with amyloid- β peptide, and prevent fibrils formation involved in Alzheimer's disease.

Abstract: We have recently demonstrated that large molecular chaperones, such as hsp60, interact with amyloidogenic proteins and interfere with the formation of fibrils. Our group is investigating structure, dynamics and mechanism of this 1.1 MDa chaperonin/prefoldin complex using a combination of NMR and EM approaches. The investigation of the active complex in presence of amyloidogenic protein will allow the observation of the transfer of unfolded protein from prefoldin to the chaperonin cavity. The student will use high field NMR spectroscopy in combination with advanced isotopic labelling to study the network of interactions between the chaperonin/prefoldin complex and amyloid- β peptide. The final goal of the project is a better understanding of how these chaperones are preventing the formation of fibrils. Furthermore, such large protein machineries will be used as novel opportunities to develop new biophysical and biochemical tools to manipulate transient oligomers of these Alzheimer related proteins.

The M2 student who joins the project will benefit from a 8 k€ scholarship and is expected to continue in doctoral studies.

Methods: Protein expression, Advanced isotopic labeling, chromatography, High Field Nuclear Magnetic Resonance, Electron Microscopy.

Up to 3 relevant publications of the team:

- Macek, Kerfah, Boeri Erba, Crublet, Moriscot, Schoehn, Amero, Boisbouvier "Unraveling Self-Assembly Pathways of the 468 kDa Proteolytic Machine TET2" **Science Adv.** 3, e1601601 (2017).
- Kerfah, Plevin, Sounier, Gans, Boisbouvier "Methyl Specific Isotopic Labeling: A Molecular Tool Box for NMR Studies of Large Proteins" **Current Opinion in Structural Biology** 32, 113-122 (2015).
- Plevin, Bryce, Boisbouvier "Direct Detection of CH/ π Interactions in Proteins" **Nature Chem.** 2, 466-471 (2010).

Requested domains of expertise (up to 5 keywords):

Structural biology, Biochemistry, Biophysics, Protein folding.