

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

Laboratory/Institute: **Institut de Biologie Structurale**  
Team: **ELMA** Head of the team: **Bruno Franzetti**

Director: **Winfried Weissenhorn**

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

**Dominique Madern and Eric Girard**

**HDR: yes for both**

**Address: Institut de Biologie Structurale, UMR 5075 CEA-CNRS-UJF-PSB  
71 avenue des Martyrs, CS 10090  
38044 Grenoble Cedex 9**

**Phone: 0 4 57 42 85 71**

**e-mail: Dominique.Madern@ibs.fr; Eric Girard@ibs.fr**

**Program the Master's degree in Biology:**

Integrative Structural Biology

**Title of the project: Allosteric regulation studies of paleo enzymes**

**Objectives (up to 3 lines):** How do enzyme properties evolved is a fundamental question. To address this question we use the resurrection of ancestral proteins for investigating the genesis of allosteric regulation in a large family of enzyme involved in the metabolism.

**Abstract (up to 10 lines):** The M2 internship is integrated within a project funded by the French National Research Agency.

How does protein sequence resurrection work? This is a stepwise process relying on the phylogeny of the studied proteins. Then, the more probable ancestral sequences at each nodes of divergence are calculated. In a last step, the inferred ancestral gene, which codes for an ancestral protein, is synthesized and expressed.

The candidate will purify and characterize enzymatic properties and allosteric behavior of ancestral dehydrogenases involved in the metabolism. The candidate will screen crystallization conditions and will collect diffraction data in order to solve their crystallographic structure.

**Methods (up to 3 lines):** Purification of protein, spectrophotometry, enzymology, crystallization methods, X-rays diffraction data collection.

**Up to 3 relevant publications of the team:** Thermal activation of 'allosteric-like' large-scale motions in a eukaryotic Lactate Dehydrogenase. Katava et al., (2017) Sci Rep. 2017 Jan 23;7:41092. Sampling the conformational energy landscape of a hyperthermophilic protein by engineering key substitutions. Colletier et al., (2012) Mol Biol Evol. 2012 Jun;29(6):1683-94. Structural Insight into Ubiquitin-Like Protein Recognition and Oligomeric States of JAMM/MPN<sup>+</sup> Proteases. Cao & Engilberge et al., (2017) Structure. 2017 May 4. doi: 10.1016/j.str.2017.04.002.

**Requested domains of expertise (up to 5 keywords):** Biochemistry, Structural biology, Crystallography