Stage M2 physique 2018

Comprendre l'évolution de l'allostérie dans une famille de déshydrogénase grâce à la structure d'enzymes ancestrales ressuscitées.

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Equipe de recherche/Research team: ELMA. **Directeur :** Franzetti Bruno

Profil du candidat souhaité: Le (la) candidat(e), titulaire d'un M1 (ou équivalent), doit faire preuve d'un intérêt fort pour les méthodes de la biologie structurale, en particulier pour la cristallographie aux rayons X. Une précédente expérience de laboratoire appliquée à la biologie structurale en M1 serait un plus. Le (la) candidat(e) travaillera en étroite relation avec une Post Doctorante spécialisée en cristallographie.

Summary: Allostery is one of the most effective mechanisms for regulating protein activity. This regulation is due to the binding of a ligand to one protein site which affects the catalytic site by long range distance effects. Numerous studies have been conducted to understand the fundamental basis of allosteric regulation. Nevertheless, some aspects of the allosteric modulation are still poorly understood. In particular, the genesis of the allosteric mechanisms remains unknown. The evolutionary structural and biochemical approach used during the M2 training period is based on ancestral protein resurrection.

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 structures. This project is supported by the Agence Nationale de la Recherche.