Institut Microbiologie, Bioénergies et Biotechnologie
Aix+Marseille Université

PhD position

Investigation into the structural dynamics-activity relationship of a novel *E.coli* chaperone of the Secretory pathway

Keywords

Bacterial chaperones, Secretory pathway, Structural dynamics, Protein-Protein interactions, Spin Labeling & EPR spectroscopy

Summary

YecA is a bacterial molecular chaperone (MC) newly identified in *E.coli* in 2020. This MC interacts with different proteins synthetized by the ribosome to maintain their unfolded state prior to their periplasmatic translocation across the membrane (Secretory pathway, Sec). Due to its recent discovery, the mechanism of client protein binding/release from a kinetic point of view including the implication of the structure has not yet been characterized for YecA.
This thesis subject aims to analyze the structural dynamic-activity relationship of YecA by integrative biophysical approaches. Isothermal Titration Calorimetry (ITC) and Dynamic Light Scattering (DLS) techniques will be used initially to investigate kinetic and thermodynamic aspects of the substrate recognition mechanism of YecA. These measurements will determine the affinity strength of YecA for its partners and discriminate between its possible holdase or unfoldase activity in the Sec pathway. The implication of the structural dynamics of YecA in its function will be further studied using Site Directed Spin Labeling (SDSL) associated to EPR spectroscopy. In vitro as well as in bacterial (in-cell) EPR experiments will be conducted to investigate YecA conformational transitions at the molecular level upon interacting with its partner proteins. Another aspect of the PhD project involves the development of innovative strategies based on a protein trans-splicing method to enlarge the domain of application of SDSL-EPR approaches. The integration of all the results will permit to decipher the chaperone activity of YecA in the Sec pathway and the link between structural dynamics and its mechanism of action. The complementary nature of the two laboratories is key to undertake this project and the PhD candidate will have the opportunity to acquire both biochemical and biophysical knowledge on proteins in an ideal scientific environment.

The co-supervisors

Valérie BELLE / Alessio BONUCCI, Laboratoire de Bioénergétique et Ingénierie des Protéines – BIP (abonucci@imm.cnrs.fr)

Déborah BYRNE, Institut de Microbiologie de la Méditerranée – IMM (byrne@imm.cnrs.fr)

Location

BIP and IMM, Campus Joseph Aiguier, Marseille, France

Doctoral school

Life and Health Sciences (ED 62), Aix-Marseille Université (https://ecole-doctorale-62.univ-amu.fr/)

Candidate profile

Candidate with background in biochemistry, biophysics and biotechnology is particularly appropriate for this PhD project. Previous practical experiences and theoretical knowledge on protein production using DNA-recombinant strategies, chromatography techniques for biomolecule purification and magnetic resonance are considered as a solid advantage. The candidate should show strong motivation and enthusiasm for the experimental research activities.

Soft skills: Autonomy, Teamwork, Good (written and oral) communication skills in English are required.

Application for an interview

In order to apply for an interview, candidates must send copies of the following documents to A.Bonucci (**abonucci@imm.cnrs.fr**) & D.Byrne (**byrne@imm.cnrs.fr**) by email before April 15th 2024:

- Curriculum Vitae (CV)
- A motivation Letter explaining his/her interest for this PhD fellowship
- A supporting letter from previous scientific supervisors
- A list of master exam grades and the specialization ranking (if available)

The candidate selected by the co-supervisors will be interviewed on June 4th 2024 by the Institute of Microbiology, Bioenergies and Biotechnology (IM2B) jury. Defense modalities will be given later.

Do not hesitate to contact the co-supervisors (A.Bonucci & D.Byrne) for more information.