Institut Microbiologie, Bioénergies et Biotechnologie
Aix*Marseille Université

PhD position in Molecular Biology/ Biochemistry

(*Laboratoire d'Ingénierie des Systèmes Macromoléculaires – LISM and Laboratoire de Bioénergétique et Ingénierie des Protéines – BIP, Marseille, France*)

Investigating the bacterial cell-penetrating and cargo capacity of cell penetrating peptides by EPR spectroscopy and fluorescence microscopy.

Keywords

Cell-penetrating peptides, EPR spectroscopy, Fluorescence microscopy, paramagnetic and fluorescent labels, *in vivo* structural studies.

Summary of the project

Protein tags bringing peculiar chemical or spectroscopic proprieties are broadly used and necessary in many modern methods, yet are hardly or impossibly encoded genetically. For example, electron paramagnetic resonance spectroscopy (EPR) applied in cells requires the incorporation of a chemically synthesized paramagnetic label onto specific protein positions. Single-molecule fluorescence microscopy would also benefit from very bright and stable chemical dye labeling, which can favorably replace genetically encoded fluorescent proteins often perturbing protein functions, yet are currently limited by the need to retain membrane permeability to enter the cell. Hence, there is a need for methods enabling the delivery of exogenously labeled proteins inside cells.

Cell Penetrating Peptides (CPPs) have the ability to transport a variety of covalently linked cargoes inside living cells, such as functional drugs against cancer cells[1]. These short peptides have the capacity to cross cellular membranes without the recognition by specific receptors. However, while several CPPs are currently available for eukaryotic cells, CPP research in bacteria has been uniquely focused on the anti-bacterial properties of CPPs in drug-resistant pathogenic bacteria. Here, we will focus on two potential "bacterial CPPs" that can serve to import exogenous proteins into bacteria without killing them: i) "CPP70", a synthetic CPP recently described to transport GFP inside *E. coli* cells,[2] ii) and the C-ter domain of a specific human protein, which gave first evidence to function as a CPP in bacteria in a recent study we conducted in collaboration with Pr. B. ZAMBELLI (University of Bologna, Italy). The project we propose is an in-depth investigation of the CPP and cargo capacity of these peptides by combining fluorescence microscopy and EPR.

Our study will have important repercussion, largely facilitating many "in-cell" applications, like fluorescence microscopy with proteins labeled with bright and stable dyes and in –cell biophysical studies (in-cell NMR, EPR, FRET) and further supports the potential of CPPs in therapeutics. Moreover, it will provide a new tool to deliver proteins and chemicals which may ultimately take the form of a delivery kit for use in bacteria.

[1]Tietz, O., et al. Nat. Chem. 2022, 14, pages 284–293. [2] HM Lee et al, Commun Biol, 2021, 4, 205.

The co-supervisors

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Doctoral school

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

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Expected profile of the candidate

The candidate should have an education background in molecular biology, biochemistry and/or cell biology. He/She must be able to demonstrate critical thinking, have good oral and written communication, in English, and be able to work as part of a collaborative project. A predilection for biophysical and/or fluorescence microscopy methods would help.

How to apply?

Send us a CV (specifying the English level), a cover letter, transcripts and ranking of Master degree (Master 1 and first semester of Master 2), and the contact information for at least two references by **April 30th 2023.**

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The candidate will be selected by the co-supervisors before May 15th, and will be interviewed on June 6th 2023 by the Institute of Microbiology, Bioenergies and Biotechnology (IM2B) jury which is financing **2 PhD positions among 4 candidates** (starting in October 2023). Defense modalities will be given later.