Institut Microbiologie, Bioénergies et Biotechnologie
Aix*Marseille Université

# PhD position

## Nanodisc: a key advantage in studying bioenergetics membrane proteins

### Keywords

Nanodiscs, cytochrome bd like -oxidase, membrane proteins, proteins lipids interactions, quinones

### Summary of the project

Membrane proteins are essential in numerous cellular processes, so they are the target of about 70% of the marketed drugs (1). Even though MPs have been investigated for decades, a blind spot in their studies remains the understanding of the interactions between them and membrane lipids (2). Combining full enzymatic characterization thanks to IM2B facilities, to cutting-edge approaches on preserving or mimicking membrane like environment, we would be able to decipher the function of a key respiratory enzyme, physiologically important in the growth of many bacteria: Cytochrome bd oxidase (cyt bd). This enzyme catalyzes the oxidation of quinol molecules to reduce O2 and to transfer protons from cytoplasm to inter-membrane space contributing to the biological energy conservation (3). As cyt bd is a prokaryote specific enzyme found in several pathogenic species, it is considered as a potential antibiotic target (4). In this context, understanding the function of cyt bd and its sensitivity to the molecular environment would be a steppingstone to designing novel antibiotics. Moreover, using the cyt bd from E. coli, Asseri et al have shown that enzyme activity is dependent on the membrane lipid environment (5). In order to explore the enzyme activities in a membrane-like environment, with all the essential lipids in the vicinity of cyt bd, lipid nanodiscs offer a very promising avenue of research.

In this project, we propose to use nanodiscs to explore the lipids sensitivity of enzymatic activity of a cyt bd. As a model system, we will use the enzyme from a non-pathogenic species, the soil bacterium Solidesulfovibrio fructosivorans (Sf). Professor James Sturgis (JS) has a recognized expertise in protein – lipid interactions and in various tools to study it: liposome, nanodiscs, detergent (6); while Eric Pilet (EP) and his close collaborator on this project, Myriam Brugna (MB) are experts in bacterial terminal oxidases purification, protein - quinone interactions and functional (enzymological and biophysical) characterization (7-10).

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*2. J. P. Duneau, J. Khao, J. N. Sturgis, Lipid perturbation by membrane proteins and the lipophobic effect. Biochimica et Biophysica Acta-Biomembranes 1859, 126-134 (2017).*

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*10. E. Pilet, A. Jasaitis, U. Liebl, M. H. Vos, Electron transfer between hemes in mammalian cytochrome c oxidase. Proc Natl Acad Sci U S A 101, 16198-16203 (2004).*

## The co-supervisors

James STURGIS, Laboratoire d'Ingénierie des Systèmes Macromoléculaires - LISM (sturgis@imm.cnrs.fr)
Eric PILET, Laboratoire de Bioénergétique et Ingénierie des Protéines – BIP (epilet@imm.cnrs.fr)

## Location

LISM and BIP, Campus Joseph Aiguier, Marseille, France

## Doctoral school

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

## Expected profile of the candidate

The candidate should have a strong expertise in protein purification and characterization by numerous structural and biophysical techniques. Some experience in working with membrane proteins and lipids would be appreciated. During the selection process, having an international experience will be considered beside academic results.

## 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 15th 2024.

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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.