PhD postition

Unraveling a new copper resistance mechanism in bacteria

Copper (Cu) is required in different key metabolisms like respiration and photosynthesis, yet Cu is cytotoxic even at low concentrations. Human activities lead to Cu accumulation in the environment that is a threat to health and ecosystems, and it contributes to the emergence of Cu resistant organisms. Understanding bacterial Cu homeostasis diversity is therefore highly relevant since it could provide valuable targets for novel antimicrobial treatments. This project aims at describing an original Cu resistance mechanism of environmental and pathogenic bacteria. This mechanism occurs under anaerobiosis or micro-aerobiosis and involves the periplasmic cuproprotein CopI and potential partners yet to be identified. CopI is highly induced by Cu and possess a scarce green type cupredoxin site. In this project, we will study the CopI proteins from three models: the environmental bacterium *Rubrivivax gelatinosus* and the pathogenic bacteria *Vibrio cholerae* and *Pseudomonas aeruginosa*. These homolog proteins exhibit differences in their three Cu-binding modules (the cupredoxin site and two other His and His/Met rich regions). To reach our objective, we will produce and purify the WT proteins as well as several mutants. The different Cu sites will be fully characterized, in particular by state-of-the-art magnetic resonance spectroscopy (EPR and NMR). Redox properties and electron transfer pathways will be studied. Two potential partner proteins, selected from genome analysis, will also be studied. These proteins will be characterized in details and protein-protein interaction with CopI will be evaluated by different means. Altogether, this project will improve knowledge on Cu proteins, Cu metabolism and how bacteria resist a Cu stress.

The PhD project will exploit metal coordination chemistry, biochemistry and spectroscopy. The student will be involved in protein production and purification, biochemistry studies, redox titrations, UV-visible and advanced EPR spectroscopy.

Keywords: Copper, Bacterial resistance, Metal stress, Bioinorganic chemistry, EPR

Expected profile of the candidate

The candidate must have a Master 2 in chemistry or physical chemistry and a strong interest of the chemistry/biology interface, with good practical skills in bioinorganic chemistry and spectroscopic techniques. We are looking for a rigorous and versatile candidate, with a capacity for teamwork and skills for written and oral communications in French and English.

Application

Send CV and motivation letter to Pierre Dorlet

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Team webpage: https://bip.cnrs.fr/groups/bip07 - PI webpage: https://bip.cnrs.fr/contact/pierre-dorlet

Expected starting date : Fall 2024 – École Doctorale des Sciences Chimiques, Aix-Marseille Université.