Post-doc position on "Spectroscopic investigation of a new copper resistance mechanism in bacteria"

Workplace : CEA-Saclay Institute JOLIOT/I2BC
Supervision : Annamaria Quaranta, Pavel Müller
Start date: 18 months, from May 2025

Context and aim of the project

Copper (Cu) is present in many enzymes involved in key metabolisms like respiration and photosynthesis. Although Cu is an essential micronutrient, it can be cytotoxic even at low concentrations. Furthermore, Cu toxicity is part of the innate immunity response to kill pathogenic bacteria, and understanding the various Cu-resistance mechanisms is important for the virulence of Human bacterial pathogens. Although only few examples of Cu homeostasis systems are fully characterized, it is now clear that many systems exist in Gram-negative bacteria; in particular, the periplasmic proteins involved are very diverse and poorly described. Interestingly, a new type of proteins involved in Cu resistance has emerged in the literature over the past two decades. CopI proteins are highly induced by Cu[1] and contain a green Cu center,[2] that might have a novel mechanism of action. We aim to investigate this redox-based process using different spectroscopic techniques, including time-resolved visible and FTIR spectroscopies. In order to characterize the electron transfer (ET) flow through CopI and between CopI and its putative partners, we will employ nanosecond transient absorption (TA) spectroscopy and FTIR step-scan technique (100 ns time resolution). The electron flow throughout our system will be studied using photoredox active Ru/Re complexes.[3] Ru/Re polypyridine complexes have been successfully used as photo-initiators in TA and FTIR studies of electron transfer in proteins, which *per se* do not contain photo-active cofactors. To achieve our goal and better control the flow of electrons in our system, we will graft the Ru/Re complex on the purified proteins close to the putative site of Cu(I) binding.

Job description

The work will be carried out at CEA Institute JOLIOT (Saclay). The post-doc will perform mechanistic investigation of the electron transfer processes combining different spectroscopic techniques such as nanosecond transient absorption, time-resolved FTIR and spectro-electrochemistry.

Candidate profile

We seek a motivated researcher holding a PhD in physical chemistry. Experience in handling biological samples will be an advantage. The candidate should be able to work within an interdisciplinary team and have excellent communication skills. Interested candidates should send a CV, cover letter and the names of two referees.

Contact: annamaria.quaranta@cea.fr; pavel.muller@i2bc.paris-saclay.fr.

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[1] A. Durand, A. Azzouzi, M.L. Bourbon, A.S. Steunou, S. Liotenberg, A. Maeshima, C. Astier, M. Argentini, S. Saito, S. Ouchane. *c*-Type cytochrome assembly is a key target of copper toxicity within the bacterial periplasm (2015) *MBio* 6, e01007

[2] A. Durand, M. Fouesnard, M.L. Bourbon, A.S. Steunou, E. Lojou, P. Dorlet, S. Ouchane. A periplasmic cupredoxin with a green T1.5 center is involved in bacterial copper resistance (2021) *Metallomics* 13, mfab067

[3] [a]M.J. Bjerrum, D.R. Casimiro, I.J. Chang, A.J. Di Bilio, H.B. Gray, M.G. Hill, R. Langen, G.A. Mines, L.K. Skov, J.R. Winkler, D.S. Wuttke. Electron transfer in ruthenium-modified proteins (1995) *J Bioenerg Biomembr* 27, 295; [b] C. Shih, A.K. Museth, M. Abrahamsson, A.M. Blanco-Rodriguez, A.J. Di Bilio, J. Sudhamsu, B.R. Crane, K.L. Ronayne, M.Towrie, A. Vlček, J.H. Richards, J.R. Winkler, H.B. Gray. Tryptophan-accelerated electron flow through proteins (2008) *Science* 320,1760