Post-doctoral position: X-Ray Absorption and Imaging investigation of the Anti Cancer Activity of Copper Ionophores

Starting date: Apr, 1st 2025
Duration: 18 months
Funding: Emergence@CNRS2025, project "ACACIa"
Location: Laboratory of Chemistry and Biology of Metals (LCBM) UMR5249 UGA-CNRS-CEA Grenoble (FR)

Description: Copper is present in trace concentration in several organisms, including humans, where it plays a crucial role in vital cell functions. As free Cu is toxic, its homeostasis at the cellular level is tightly regulated. Cu also plays a role in tumor development and progression. As of today, the mechanisms ruling these phenomena are only partially known.

Our consortium investigates a novel therapeutic strategy against cancer, based on the disruption of Cu homeostasis using Cu(I)-ionophores, *i.e.* molecules that can mobilize intracellular Cu(I). Our partners at the Université Libre de Bruxelles (ULB) developed Calix[4]arenes with two imidazole groups, which efficiently bind Cu(I) and transport it across lipid bilayers.[1] We proved that these ionphorores can kill several cancer cell lines, and patented them under the name of Cuphoralix.[2] We are developing derivatives in order to seek for compounds with more specific targeting, and testing their anti-cancer efficacy.

The goal of this postdoctoral project is to unravel the mechanism of action of Cu(I)-ionophores by making use of X-ray Absorption Spectroscopy (XAS) and synchrotron-X-Ray Fluorescence (XRF) imaging, in order to help the design of future generation anticancer therapies. By XAS and XRF elemental imaging, we will interrogate Cu in Cu(I)-ionophore complexes and in various cancer cells lines treated with ionophores. This will allow us to assess the chemistry of Cu in healthy *vs* cancer cells, and the modifications of the latter induced by the ionophores *in cellulo*. The postdoctoral fellow will participate to the sample preparation for synchrotron experiments in cryogenic conditions, acquire XAS and XRF imaging data at the ESRF, and analyze them with existing, open source software.

Work environment: The selected applicant will join the Computational Chemistry, Modelling, and X-ray (CoMX, https://www.cbm-lab.fr/en/Pages/COMX/Presentation.aspx) team of the Laboratory CBM. The hosting group has a long-lasting expertise in the study of the fate of engineered metal-based (nano)materials in biological systems.[3,4] The postdoctoral fellow will work in close collaboration with the LCBM/Met&Or team of the LCBM, where the cellular and molecular biology experiments related to this project will be performed.

References: [1] Renier et al. Chem. Commun. 2020, 56, 8206. [2] Busser et al. Patent number: EP4406939A1 (filed Jan. 2023). [3] Veronesi et al. ACS Appl. Mater. Interfaces 2019, 11, 35630. [4] Rekik et al. Environ. Sci.: Nano, 2023,10, 1842.

Skills: The candidate should hold a PhD in physics, chemistry, or a related discipline. Experience with XAS and/or XRF imaging experiments and data analysis is required, if applied to biology/biochemistry it would be an asset. Previous participation to cross-disciplinary projects, proved by publications, would be appreciated.

Application: through the CNRS portal: https://emploi.cnrs.fr/Offres/CDD/UMR5249-GIUVER-001/Default.aspx?lang=EN. Deadline Dec, 16th 2024.

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