Postdoctoral Research Associate position within a France-USA collaborative Project funded by A*MIDEX.

DeNovoCatalysts, an international collaborative Project (France-USA) funded by A*MIDEX, the Aix-Marseille University Foundation, aims to develop self-assembling and water-soluble artificial mini-proteins with bioinspired heme&Trp redox cofactors for targeted catalysis, and resulting in novel versatile catalysts with enhanced reactivity for medical and/or environmental applications. Such mini-catalysts are inspired on natural metalloproteins in which their reactivity is expanded by the concerted chemistry of transition metals and protein-based radicals [1]. Our bioinspired artificial catalysts will be conceived and characterized as *in vitro* tunable model systems for understanding better the molecular determinants underlying natural catalytic strategies of drug-target heme enzymes and their bioresistance. Moreover, we will target challenging *in vivo* applications by developing the heme&Trp artificial catalysts for *in-cell* reactivity, thus emulating KatGs (His-ligated heme enzymes; pro-drug activation) or cyt P450 oxygenases (Cys-ligated heme enzymes; selective oxidation of inert C-H bonds). Our approach of engineering redox-active Trp(s) resulting in controlled Trp radical(s) as substrate oxidizing site(s) and/or electron transfer (as in KatGs natural enzymes [1]) relies on our recently developed *de novo* heme-only miniature functional proteins, using self-assembling α-helical scaffolds [2].

We are looking for a highly motivated biochemist, with a PhD in Biochemistry, Chemistry or Physics, and a strong background in biochemistry, enzyme catalysis and spectroscopy, excellent communication skills and being eager to work collaboratively in our multidisciplinary research project (Bioinorganic Chemistry, Biophysics, molecular/cell Biology), to undertake a PDRA position of 12 months (renewable based on common agreement). Competitive salary will be defined by Aix-Marseille University's salary grid and considering previous research experience. The AMIDEX International funds require that the candidate would not have obtained his/her PhD Diploma from Aix-Marseille University. The PDRA will work within the collaborative Research Project "DeNovoCatalysts" between Dr. Anabella Ivancich (Research Unit UMR 7281, CNRS & Aix Marseille University, Marseille, France), Dr. Stéphane Canaan (Research Unit UMR 7255, CNRS & Aix Marseille University, Marseille, France) and Prof. Vincent L. Pecoraro (Department of Chemistry, University of Michigan, Ann Arbor, USA).

The PDRA candidate is expected to actively take part in the expression and purification of the natural KatGs and artificial heme-binding catalysts [1]. Characterization of the purified artificial proteins (*in vitro*), binding mode(s) of the heme cofactor and comparison of the catalytic intermediates and enzymatic reactivities of the artificial proteins, bearing a heme and Trp redox cofactors, with the natural KatG enzymes from *M. abscessus*, *M. tuberculosis* and *B. pseudomallei*, will be performed. Further *in-cell* studies of the isoniazid reactivity of the successful artificial scaffolds will be carried out in *M. abscessus*, in which the KatG protein showed lower affinity to INH and substantially lower enzymatic capacity for the conversion of INH into the active form, hence resulting in naturally resistant *mycobacterium* strain [3, 4]. Experience on either natural or artificial heme enzymes, as well as protein-based radicals as cofactors in enzyme catalysis, protein biochemistry, expression and purification of metalloproteins from prior research work during PhD or postdoctoral training will be highly appreciated. Applications (including a detailed CV, a motivation letter and two letters of recommendation) should be sent to Dr A. Ivancich (aivancich@imm.cnrs.fr) before October 4th, 2 pm. Inquires can be addressed to Drs. A. Ivancich and S. Canaan (canaan@imm.cnrs.fr).

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3. Reingewertz TH, Meyer T, McIntosh F, Sullivan J, Meir M, Chang Y-F, Behr MA, Barkan D. (2019). Differential sensitivity of mycobacteria to isoniazid is related to differences in KatG-mediated enzymatic activation of the drug. *Antimicrob Agents Chemother 64*: e01899-19. DOI: 10.1128/AAC.01899-19.
4. Madani A, Ridenour JN, Martin BP, Paudel RR, Abdul Basir A, Le Moigne V, Herrmann JL, Audebert S, Camoin L, Kremer L, Spilling CD, **Canaan S**, Cavalier JF. Cyclipostins and Cyclophostin Analogues as Multitarget Inhibitors That Impair Growth of *Mycobacterium abscessus. ACS Infect Dis.* **2019** *5*, 1597-1608.