Metalloenzyme engineering for catalysis

A PhD position (expected starting date: 2019, October 1st) is available at the "Institut des Sciences Moléculaires de Marseille" (iSm2, UMR 7313) within the frame of an ANR-funded project led by Dr. Christophe Decroos.

Keywords: *metalloenzyme, artificial enzyme, protein engineering, biocatalysis, bioinorganic chemistry*

Project:

Biocatalysis harnesses the potential of enzymes in terms of selectivity (chemo-, regio-, and stereoselectivity) to transform chemicals into high-added value products under mild conditions, meeting most criteria of green chemistry. Although enzymes used as biocatalysts might suffer from several drawbacks (limited substrate scope, low efficiency) as compared with chemical catalysts. Additionally, the scope of enzymes used in industrial processes remains limited to a few class of transformations. On the contrary, transition metal catalysis has become an essential tool in modern organic synthesis and offers the access to a wide range of new transformations. Therefore, expanding the enzyme toolbox to reactions that are unprecedented in Nature could foster the implementation of new biocatalysts within biocatalytic cascades for the production of fine chemicals. Artificial metalloenzymes are expected to enlarge the chemical space accessible to enzymes by merging biocatalysis with transition metal catalysis that offers a vast repertoire of reactivity not encountered in Nature. Engineering novel reactivity within a protein can be performed by anchoring an abiotic metallic cofactor into a protein scaffold, exploiting the metal and catalytic promiscuity of metalloenzymes, or repurposing existing metalloenzymes for abiological reactivity.[1] Using the latter approach, a compelling array of carbene / nitrene transfer biocatalysts based on heme protein scaffolds (pioneering work led by Frances H. Arnold and coworkers)[2] have been developed by directed evolution for the creation of C-X bonds (X=C, N, O, S, Si, B).[3]

Within this project, we aim at repurposing the activity of another class of metalloenzymes to develop new biocatalysts catalyzing reactions not encountered in Nature. The enzyme active site will be engineered to explore metal promiscuity (especially abundant first-row transition metals). Variants will be screened for promiscuous abiological reactivity. For selected activities, the catalytic efficiency, substrate scope, and selectivity of best variants will be improved by directed evolution. Finally, the best biocatalysts will be used for the chemoenzymatic synthesis of molecules of interest.

The PhD candidate will join the BiosCiences group at iSm2 (Marseille). This group has a strong expertise in the study of metalloenzymes and the development of new (bio)catalysts.[4] The PhD candidate will evolve in a multidisciplinary environment (chemistry / biology / biophysics) and will gain experience in a range of techniques used in this project at the interface of chemistry and biology.

Candidate profile:

Highly motivated candidates (master degree or equivalent with excellent academic records) with a background in molecular chemistry and / or biological chemistry are strongly encouraged to apply. Previous laboratory experience in biocatalysis, homogenous metal catalysis, or any other field that could benefit the project would be valuable but is not mandatory.

For additional information about the project and / or the recruitment process, please contact Dr. Christophe Decroos (christophe.decroos@univ-amu.fr), but note that any application has to be submitted online *via* the CNRS job portal (http://bit.ly/2NdWvV0). The application should include a CV, a cover letter, contact information for at least two references, and academic transcripts.

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[1] Schwizer, F *et al.* (2018) *Chem. Rev.* 118(1):142-231.
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[3] a) Brandenberg, OF *et al.* (2017) *Curr. Opin. Biotechnol.* 47:102-111. b) Zhang, RK *et al.* (2019) *Curr. Opin. Chem. Biol.* 49:67-75.
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