Peptidyl metal complexes for catalysis in water

Offer description:

A 3-year PhD fellowship is available at the Biomolecules Laboratory (ENS, Paris) to work under the supervision of Nicolas Delsuc in the group "Metals in biology and redox homeostasis".
Website: https://ens-bic.fr/

Project:

Peptides are of great interest as ligands for metal complexes development since they are easy to synthesize, they are chiral, water soluble and, depending on the sequence, different coordinating groups can be introduced. Peptidyl metal complexes have been thus developed successfully as catalysts for reactions such as hydrogen transfer,[1] oxidation,[2] epoxidation,[3] aldolisation[4] and oxygenase-type transformations.[5] Interestingly these reactions were performed in water and in some cases good enantioselectivities could be reached thanks to the chirality of the peptidyl ligand.[1,4,5] Peptidyl metal complexes mimicking antioxidant metalloenzymes have also been developed to reproduce the beneficial activities of the metalloenzymes (Fig. 1).[6–9] Owing to their good biocompatibility these complexes could be used in more relevant biological systems, namely in cellular models involving oxidative stress.[7,8]

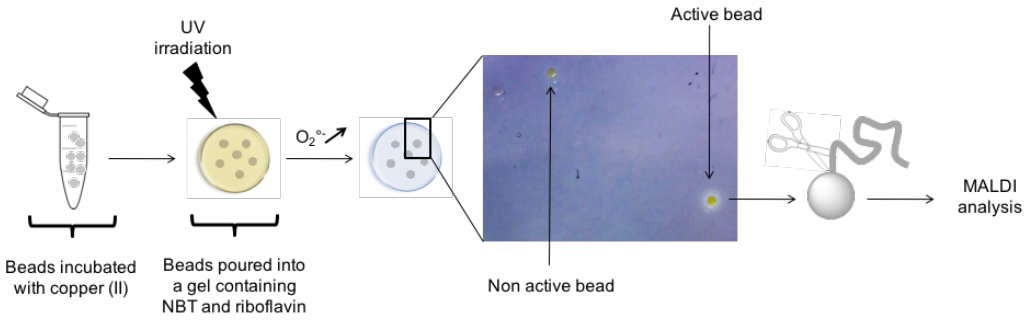

Fig. 1. Example of the screening strategy for SOD mimics discovery

In this project we will use a combinatorial strategy combined with activity-based assays to find efficient catalysts for reactions such as lytic oxidations or oxidative couplings involving CH activation. Also, mimics of nitrites reductases will be investigated. The selected complexes will be then studied in details to characterize their catalytic activities in solution, and when suitable in cells.

References (our references in blue):

(1) Dolan, M. A.; Basa, P. N.; Zozulia, O.; Lengyel, Z.; Lebl, R.; Kohn, E. M.; Bhattacharya, S.; Korendovych, I. V. Catalytic Nanoassemblies Formed by Short Peptides Promote Highly Enantioselective Transfer Hydrogenation. *ACS Nano* **2019**, *13* (8), 9292–9297. https://doi.org/10.1021/acsnano.9b03880.

(2) Bacchella, C.; Dell'Acqua, S.; Nicolis, S.; Monzani, E.; Casella, L. A Cu-Bis(Imidazole) Substrate Intermediate Is the Catalytically Competent Center for Catechol Oxidase Activity of Copper Amyloid-β. *Inorg. Chem.* **2021**, *60* (2), 606–613. https://doi.org/10.1021/acs.inorgchem.0c02243.

(3) Fingerhut, A.; Vargas-Caporali, J.; Leyva-Ramírez, M. A.; Juaristi, E.; Tsogoeva, S. B. Biomimetic Non-Heme Iron-Catalyzed Epoxidation of Challenging Terminal Alkenes Using Aqueous H2O2 as an Environmentally Friendly Oxidant. *Molecules* **2019**, *24* (17), 3182. https://doi.org/10.3390/molecules24173182.

(4) Zaithun, B. S.; Emilia, A.; Mohamed, T. M. I.; Anne, C. K.; Basyaruddin, A. R. M. Histidine-Based Copper Tetrapeptides as Enantioselective Catalysts for Aldol Reactions. *RSC Adv.* **2018**, *8* (59), 34004–34011. https://doi.org/10.1039/C8RA06814C.

(5) Cussó, O.; Giuliano, M. W.; Ribas, X.; Miller, S. J.; Costas, M. A Bottom up Approach towards Artificial Oxygenases by Combining Iron Coordination Complexes and Peptides. *Chem. Sci.* **2017**, *8* (5), 3660–3667. https://doi.org/10.1039/C7SC00099E.
(6) Csire, G.; Timári, S.; Asztalos, J.; Király, J. M.; Kiss, M.; Várnagy, K. Coordination, Redox Properties and SOD Activity of Cu(II) Complexes of Multihistidine Peptides. *Journal of Inorganic Biochemistry* **2017**, *177*, 198–210. https://doi.org/10.1016/j.jinorgbio.2017.08.033.
(7) Vincent, A.; Fores, J. R.; Tauziet, E.; Quévrain, E.; Dancs, Á.; Conte-Daban, A.; Bernard, A.-S.; Pelupessy, P.; Coulibaly, K.; Seksik, P.; Hureau, C.; Selmeczi, K.; Policar, C.; Delsuc, N. An Easy-to-Implement Combinatorial Approach Involving an Activity-Based Assay for the Discovery of a Peptidyl Copper Complex Mimicking Superoxide Dismutase. *Chem. Commun.* **2020**, *56* (3), 399–402. https://doi.org/10.1039/C9CC07920C.
(8) Coulibaly, K.; Thauvin, M.; Melenbacher, A.; Testard, C.; Trigoni, E.; Vincent, A.; Stillman, M. J.; Vriz, S.; Policar, C.; Delsuc, N. A Di-Copper Peptidyl Complex Mimics the Activity of Catalase, a Key Antioxidant Metalloenzyme. *Inorg. Chem.* **2021**, *60* (13), 9309–9319. https://doi.org/10.1021/acs.inorgchem.0c03718.
(9) Ben Hadj Hammouda, Y.; Coulibaly, K.; Bathily, A.; Teoh Sook Han, M.; Policar, C.; Delsuc, N. Improvement of Peptidyl Copper Complexes Mimicking Catalase: A Subtle Balance between Thermodynamic Stability and Resistance towards H2O2 Degradation. *Molecules* **2022**, *27* (17), 5476. https://doi.org/10.3390/molecules27175476.

Profile and skills:

This project involves peptide synthesis, metal complex synthesis and catalysis. Therefore, a strong background and experience in organic synthesis is required.
Knowledge in inorganic chemistry would be appreciated.
The candidate will be able to communicate scientific results in a clear and rigorous manner, including in English.
He/she will have to show good manners and will be involved in the collective life of the laboratory.

Selection Process:

Refer to the following link: http://www.ed406.upmc.fr/fr/contrats-doctoraux/depot-des-candidatures.html
Dead-line: May, 12th