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Team ALAMBIC
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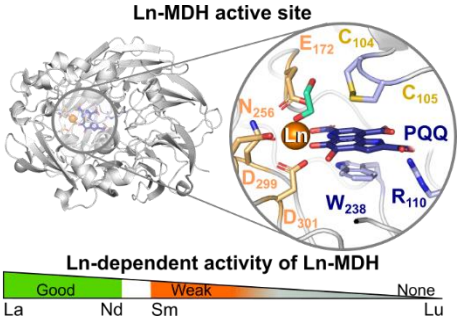
PhD Position

Synthesis of bio-inspired lanthano-peptide catalysts

Keywords: organic synthesis, peptide synthesis, lanthanide complexes, bio-inorganic chemistry

Project: Lanthanides (Ln) recently joined the family of elements essential to living organisms.[1] The first Ln-enzyme, a methanol dehydrogenase, has been identified. In addition to the redox cofactor pyrroloquinoline quinone (PQQ) responsible for the oxidation of methanol, Ln-MDH contains in its active site a Ln^{3+} ion bound to PQQ (**Figure**). Intriguingly, the catalytic activity of this enzyme strongly depends on Ln^{3+}. It is the most active with early Ln^{3+} (La-Nd), and has no detectable activity with late Ln^{3+}. Due to the difficulty to study the enzyme itself, two alternative approaches have been investigated: (i) the synthesis of molecular complexes mimicking the Ln-PQQ complex;[2] (ii) the use of bio-engineered proteins.[3] In both cases, the catalytic activities were poor to moderate.



The strategy proposed in this project is to combine the advantages of both approaches, thanks to the synthesis of libraries of Ln-binding peptides. Indeed, the choice for a peptide scaffold enables a fast and modular synthesis (as for molecular complexes) and is easily tunable by selecting the appropriate amino acids (as for proteins). The main goal of the project is to obtain structural mimics of the enzyme. The work will be divided in three parts:

- **(i)** **Synthesis of non-natural amino acids** by organic synthesis, either for Ln-binding or PQQ-coupling;
- **(ii)** **Synthesis of peptides library** by solid phase peptide synthesis with scaffolds of increasing complexity;
- **(iii)** **Physico-chemical analyses** (UVvis, luminescence, circular dichroism, NMR) to characterize Ln^{3+}-coordination sphere and peptides stability and structure.

Environment: The successful candidate will work in an exciting, dynamic and international environment at the Coordination Chemistry Laboratory of the CNRS in Toulouse, France, in the team ALAMBIC. The technical and scientific environment is of high quality and fully adequate for the realisation of the project.

Profile: We are looking for a highly motivated student with a background in molecular chemistry, strong synthetic skills and excellent grades. Applicants should have a strong interest in multidisciplinary projects in the field of bio-inorganic chemistry. In addition, ability to write a scientific report, and strong teamwork skills are required.

Application: Please, send your resume, academic records and two references to emilie.mathieu@lcc-toulouse.fr.

References

[1] a. Daumann, L. J. Essential and Ubiquitous: The Emergence of Lanthanide Metallobiochemistry. Angew. Chem. Int. Ed. **2019**, 58 (37), 12795–12802; **b.** Featherston, E. R.; Cotruvo, J. A. The Biochemistry of Lanthanide Acquisition, Trafficking, and Utilization. Biochim. Biophys. Acta BBA - Mol. Cell Res. **2021**, 1868 (1), 118864.

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