Binding Site Properties versus Intramolecular Cooperativity in Lanthanide and Actinide Recognition by the N-terminal Domain of Calmodulin

A PhD position is opened at the Bioscience and Biotechnology Institute Aix Marseille (BIAM) team Interactions Protéine Métal (IPM) located at the CEA-Cadarache, within a joint project and co-direction with the Laboratory of Actinide-Ligand Interactions (LILA) at CEA Marcoule. co-direction C. Berthomieu catherine.berthomieu@cea.fr and L. Berthon laurence.berthon@cea.fr

Lanthanides (Ln), which belong to the Rare Earth Elements (REEs), are critical raw materials for Europe because of their key role in energy, transport and communication technologies. Developing more selective and sustainable extraction processes is therefore essential for recycling and recovering REEs from complex secondary resources. However, separating lanthanides from one another, or from chemically similar minor actinides such as americium (Am(III)), remains a major challenge because of their closely related coordination chemistry.

Metal-binding proteins provide an attractive bioinspired alternative to conventional extractants by offering genetically encoded and tunable metal-recognition sites. Recent discoveries, including lanmodulin, have demonstrated that proteins can bind lanthanides with remarkable affinity. Recent results from the BIAM/IPM and DES/LILA teams reported also a high-affinity binding site for Ln(III) (logK = 9–12) for an engineered EF-hand motif at site 1 of the N-terminal domain of calmodulin (Berthomieu et al. 2026 EurJIC 10.1002/ejic.202500468). Unlike lanmodulin, the N-terminal domain of calmodulin constitutes a simple two-EF-hand model system that enables the tuning and quantitative analysis of binding-site properties and intramolecular cooperativity, providing a unique framework to decipher the molecular determinants of affinity and selectivity.

This PhD project aims to identify the molecular determinants governing affinity, intra-lanthanide selectivity and Ln(III)/Am(III) discrimination. The project will notably investigate how modifications of the amino acid sequence at one or both EF-hand sites influence metal recognition and cooperative binding. Smaller engineered proteins and peptides will also be developed to optimize metal capture and enable structural characterization by solution NMR.

The project combines AI-guided protein engineering, focused directed evolution, molecular dynamics simulations, structural biology and advanced spectroscopic techniques (fluorescence, TRLFS, FTIR, ITC, NMR and X-ray crystallography). It will provide new insights into protein–f-element recognition while establishing design principles for next-generation bio-based ligands dedicated to the sustainable recovery of strategic metals.

We are seeking candidates holding a Master's degree or an engineering degree in chemistry, biochemistry, chemical biology or a related discipline, with an interest in protein engineering, bioinorganic chemistry and interdisciplinary research at the chemistry–biology interface. The PhD position is fully funded and will start on October 15, 2026. The successful candidate will be based primarily at BIAM (CEA Cadarache) within the IPM team, with regular interactions with the LILA team (CEA Marcoule).

Interested candidates are invited to submit a CV, a cover letter, and the name of two referee to catherine.berthomieu@cea.fr and laurence.berthon@cea.fr