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Laurence Berthon-Nigond, Claude Berthon

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Study of the interaction between actinides and peptide ligands

FAUX Emilien^a, DARONNAT Loïc^a, SAUGE-MERLE Sandrine^b, BERTHOMIEU Catherine^b, BERTHON Claude^a, BERTHON Laurence^a

(a) CEA, DES, ISEC, DMRC, Univ. Montpellier, Marcoule, France

(b) Aix-Marseille Univ., CEA, CNRS, BIAM, UMR7265, IPM, 13108 Saint Paul-Lez-Durance, France

Actinides are radioactive metals of high importance in civil and military nuclear activities. Trace amounts of these elements may be found in the environment due to historical nuclear tests and accidental releases. Most actinides being alpha emitters, it is essential to investigate their behavior within the human body. While the targeted organs are well-known, the transport mechanism and molecular interactions remain unidentified. Proteins have been identified as actinide targets in the event of human contamination. Although the literature on the interactions between actinides and proteins is scarce, metalloproteomic studies have shown that several calcium-binding proteins have a strong affinity for actinides¹. As a model for all calcium-binding protein, the **calcium-modulated protein** (calmodulin) was chosen for its EF-hand motif site, which is widely present in calcium-binding proteins, and its high importance in cellular regulatory function. L. Daronnat investigated the interaction of plutonium (IV) with several variants of the calmodulin and observed various behaviors of the plutonium depending on the variant of calmodulin used²: the formation of a Pu(IV)-calmodulin complex, the formation of a Pu(III)-calmodulin complex and the formation of hexanuclear clusters of plutonium. CaME (Engineered Calmodulin) is a variant of calmodulin developed especially to bind plutonium(IV). This variant has an extra carboxylate ligand in its complexation loop (shown in figure 1), increasing its affinity for actinides IV.

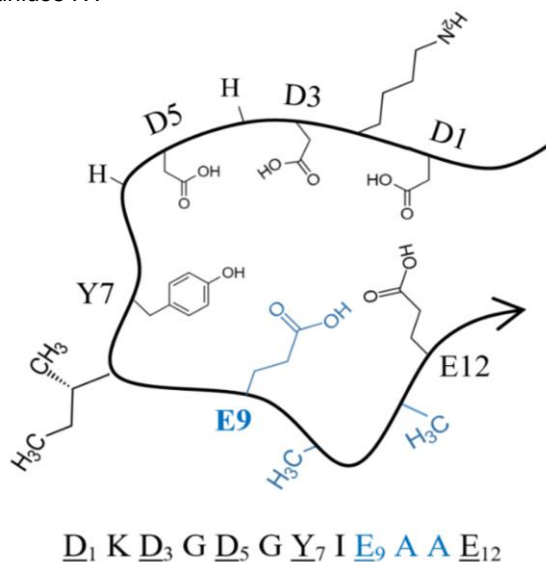


Figure 1 – Structure and sequence of the coordination site of CaME

This particular variant was the only which did not promote the formation of plutonium clusters. Instead, it only generated 1:1 complexes. Additionally, an unexpected change of the oxidation state of plutonium (from IV to III) was noticed in presence of CaME.³ To get a better understanding of this behavior, a deepened characterization of the species formed between CaME and actinides have been undertaken.

This work aims to characterize the complexes formed between CaME and actinides (Th, U, Np, Pu), using different experimental techniques. Electrospray Ionization Mass Spectrometry was used to determine the stoichiometry of the complexes and UV-Vis-NIR Spectroscopy was used to characterize the environment of the actinide. Structural data were obtained through two or three-dimensional NMR spectroscopy. For that, an extra batch of CaME was synthesized and enriched with ¹³C and ¹⁵N, allowing for ¹H-¹³C-¹⁵N NMR analysis.

The paramagnetic properties of the plutonium are used to identify the amino acid involved in the coordination sphere of the metallic ions.

- (1) Aryal, B. P. *J. Proteomics* **2012**, 75 (5), 1505–1514
- (2) Daronnat, L. Doctorat Ph D thesis of the Montpellier University, **2023**
- (3) Daronnat, L. *Inorg. Chem.* **2023**, 62 (21), 8334–8346