

Chemical biology approaches to investigate metal-protein interactions: the case of f-elements

Sarah Hostachy

Laboratoire Systèmes Moléculaires et nanoMatériaux pour l'Energie et la Santé (SyMMES)
UMR 5819 (UGA – CEA – CNRS – Grenoble-INP)
17 avenue des Martyrs, 38054 Grenoble Cedex 09, France
sarah.hostachy@cea.fr

Recent technological developments have expanded and intensified the use of metals, including f-block elements (lanthanides and actinides), in domains as diverse as energy, digital technologies, and medicine. Their current ubiquity increases the likeliness of human or environmental exposure, raising the question of their impact on life.^{1,2} Understanding the interactions of these metals with living systems at the molecular level is thus needed to inform detoxification strategies, but also to inspire innovative bio-driven approaches for their recycling and remediation.³ Among biomolecules, proteins play a key role in the cellular response to environmental changes, and are thus interesting metal targets to investigate. Yet, identifying metal-protein interactions is particularly challenging in the case of f-elements, due to the highly electrostatic character of these interactions.⁴

Our group develops molecular tools to identify and characterize metal-protein interactions in the case of uranyl and lanthanides. We designed a series of biomimetic peptides to investigate the binding of human proteins to the uranyl cation. We also designed an original uranyl-binding fluorescent probe with affinity for uranyl in the range of those of native proteins. Together, these tools enabled us to develop a simple assay to measure uranyl-binding affinity of proteins.⁵ We are now aiming to develop strategies for the identification of f-element-protein interactions in a cellular context.

¹ Pallares *et al.* *Proc. Natl. Acad. Sci.* **2021**, 118 (18).
<https://doi.org/10.1073/pnas.2025952118>.

² Vidaud *et al.* *Chem Res Toxicol* **2012**, 25 (6), 1161–1175.
<https://doi.org/10.1021/tx300064m>.

³ Mattocks *et al.* *Chem. Soc. Rev.* **2020**, 49 (22), 8315–8334.
<https://doi.org/10.1039/D0CS00653J>.

⁴ Hagege *et al.* *Trac-Trends Anal. Chem.* **2015**, 64, 64–74.
<https://doi.org/10.1016/j.trac.2014.08.013>.

⁵ Laporte *et al.* *Angew. Chem. Int. Ed.* **2022**, 61 (26), e202203198.
<https://doi.org/10.1002/anie.202203198>.