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The role of phosphorous biochemistry in actinide human contamination

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In case of accidental exposure to radioelements, internal actinide toxicity is related to both emitted radiation and to the in-vivo circulation scheme. Blocking the biological pathways of the actinides in the human (or more generally mammalian) systems and/or increasing their elimination rate would considerably decrease the toxicity of these elements. Overall the need for a better understanding of the actinide pathways in biological systems is of fundamental importance with regards to the assessment of nuclear risk. The use of biomimicking molecules or molecular building blocks (like simple aminoacids with important chelating groups, small peptides etc.) is one of the methods to better understand these chemical pathways that drive actinide incorporation into cells and organs. Our present strategy has focused on the cation coordination itself in a so-called bioactinidic approach corresponding to actinide chelation by important biological actors or building blocks of biological molecules that may be considered as simplified mimicking actors. Note that actinide chemistry is complicated by complex RedOx behavior and large ionic size radius that induces significant changes in ligand conformation with respect to the essential biological cations such as iron. These complications are why a fundamental and simplified approach to the question of actinide transfer in biological systems is essential.
The phosphate chemical function is ubiquitous in biological systems. The phosphorylations of proteins are transient phenomena, which play a key role in the signalization cascades, and actinide bound to the phosphorylated groups might disturb some biochemical pathways. While it is involved in phosphorylated proteins phosphates are also the major functions of the nucleotides. Consequently phosphorylated amino acid building blocks as well as phosphorylated proteins may be considered as possible targets for actinide complexation in the various compartments of the biological machinery. This was evidenced in previous studies aiming at identifying proteins able to bind uranyl starting from cell extracts.
This presentation will give a background of actinide bioinorganic chemistry in the framework of nuclear toxicology. It will in particular browse examples of actinide coordination mechanisms with two distinct biological systems that involve phosphorylated biomolecules. The first one is the nucleotide family, which is involved in many enzymatic reactions but also as essential building blocks in the nucleic acids. The second one is a targeted protein involved in the skeleton turnover, namely osetopontin (OPN). We have in parallel investigated an hexapeptide that is representative of the active site of osteopontin on the bond surface.
Three actinide cations will be discussed: thorium(IV) as a representative of actinide(IV), uranyl(VI) as the most ubiquitous example of actinyl oxocations and americium(III) as a representative of oxidation state +III and middle actinides. In addition, lutetium(III) will be also discussed as a chemical analogue of the middle actinides.

Primary author: Prof. DEN AUWER, Christophe (University Nice Sophia Antipolis, Nice Chemistry Institute)

Co-authors: Dr VIDAUD, Claude (CEA Marcoule DSV/iBEB); Dr CREFF, Gaëlle (University Nice Sophia Antipolis, Nice Chemistry Institute); Dr CHARBONNEL, Marie Christine (CEA Marcoule DEN/DRCP/SCPS); Dr SOLARI, Pier Lorenzo (Synchrotron SOLEIL); Dr SAFI, Samir (University Paris Orsay, IPN); Dr MOSTAPHA, Sarah (CEA Marcoule DEN/DRCP/SCPS)

Presenter: Prof. DEN AUWER, Christophe (University Nice Sophia Antipolis, Nice Chemistry Institute)

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