Direction
des **ressources humaines**
Université de Strasbourg

Position description

1. Position identification

Title of post : Post-doctoral researcher

Type of contract : Post-doctoral contract

Category (A,B or C) : A

Contract/project period : 12 months **Expected date of employment :** January 2025

Proportion of work : Full time

Workplace : Institut de Chimie de Strasbourg (team CLIC)

Desired level of education : PhD

Experience required : PhD defended less than a year ago

Contact(s) for information on the position (identity, position, e-mail address, telephone) :

Jean-Claude Chambron, CNRS Research Director, jcchambron@unistra.fr, +33(0)368851534

Date of publication : November 28, 2024

Closing date for the receipt of applications : December 26, 2024

2. Research project or operation

The post-doctoral research project will be carried out in the frame of the French-German ANR/DFG ActiDecorp project.

3. Activities

➢ **Description of the research activities :**

Heavy metals released in the environment are toxic, because they bind to proteins devoted to the storage of essential metal cations, and/or they replace these in the respective metalloenzymes. In addition to their chemical toxicity, radioactive heavy metals are dangerous, because they emit high energy radiations, which, among other effects, can generate deleterious free radicals. Nevertheless, if mastered in terms of energy, intensity, and location, nuclear radiations can be useful: This is the purpose of nuclear medicine, which uses them for diagnostic and curative needs.

In order to remove toxic metals from the organism or handle toxic metals *in vivo*, it is necessary to use small molecules called chelators, which must show favorable complexation thermodynamics and kinetics, and sequester the metal cation from its surroundings.

In this project, we shall target highly toxic actinide (An) metals such as plutonium and americium, and terbium, a lanthanide (Ln) with four potentially useful radioisotopes for nuclear medicine.

There are two FDA approved chelators for the chelation therapy of An, and nuclear medicine, diethylenetriaminepentaacetate (DTPA) and dodecanetetraacetate (DOTA), respectively. They are well adapted to the sequestration of the heavy metals, however, not optimally: DTPA lacks selectivity for the An, forming stable complexes with the biological cations Fe^{3+} and Cu^{2+}; DOTA strongly complexes Tb^{3+}, but because of the small size of its cavity, the complexation reaction must be carried out at high temperature, which is not compatible with the use of antibody-conjugated chelators. Therefore there is an urgent need for new chelators able to replace DTPA and DOTA.

Our aim is to develop macrocyclic chelators with a cavity flexible enough to readily incorporate the An or Ln metal cation, and functionalized with bidentate arms in order to satisfy its high coordinence. The chelators will be modular in order to control the hard/soft Lewis basicity balance, the harder and softer donor atoms being better adapted to the M^{4+} and M^{3+} cations respectively.

This work will be performed in the context of two international collaborative projects. Chelation therapy will involve the IRSN in Paris for the *in vitro* and *in vivo* biological tests, and the HZDR in

Dresden (Germany) for the An coordination chemistry; nuclear medicine (molecular imaging and radiotherapy) experiments will be carried out at the Lausanne University Hospital (CHUV).

➢ **Related activities :**

- Presentation of the results in the frame of seminars and conferences
- Involvement in writing up publications

4. Skills

➢ **Qualifications/knowledge :**

- Good theoretical and experimental knowledge in organic synthesis
- Good knowledge of organic synthesis
- Knowledge of coordination chemistry

➢ **Operational skills/expertise :**

- Mastering of the techniques of organic synthesis (reaction implementation and work up, product purification
- Mastering of flash column chromatography
- Experience in LC-MS and reverse phase HPLC

➢ **Personal qualities :**

Dynamism, rigor, motivation, strong capacity of personal investment

5. Environment and context of work

➢ **Presentation of the laboratory/unit :**

The Institute of Chemistry of Strasbourg is a joint research unit associated with the University of Strasbourg and the CNRS (UMR 7177). It includes about 20 research groups with expertise in organic chemistry, coordination chemistry, supramolecular chemistry, biochemistry, catalysis, and theoretical chemistry. The Institute of Chemistry of Strasbourg belongs to the Le Bel Research Federation, which shares analytical platforms tNMR, X ray diffraction, mass spectrometry, elemental analysis, electronic emission spectroscopy, circular dichroism, etc.)

➢ **Hierarchical relationship :**

Jean-Claude Chambron is the responsible of the partner "University of Strasbourg" of the ANR/DFG ActiDecorp project, and will directly supervise the work of the recruted person. The work will be executed within the CLIC group (Coordination, Ligands, Interactions, and Catalysis) of the Institute of Chemistry of Strasbourg, the head of which is Victor Mamane, Reserach Director at the CNRS

➢ **Special conditions of practice (notice attached):** none

To apply, please send your CV, a motivation letter and the names of two reference persons : jcchambron@unistra.fr