POST-DOCTORAL POSITION

Université de Bretagne Occidentale, Brest, France
UMR CNRS 6521

Synthesis and coordiantion study of new macrocyclic-based HOPO chelates for molecular imaging

Description of the project. Molecular imaging allows the visualization of cellular functioning or the monitoring of the molecular process in living organisms without disturbing them. However it requires imaging probes for more efficiency. PET and TEMP nuclear imaging techniques were the first molecular imaging modalities used clinically. These two imaging modalities, which are particularly well known for their use in clinical oncology, also renders possible to carry out images of molecular targets (hormonal receptors) by using appropriately vectorized probes, to mark the deposition of amyloid plaques (responsible of Alzheimer's disease) or to acquire images of hypoxic processes.

In this context of vectorized imagery, the short lifetime of ^{18}F ($t_{1/2}$ = 110 min) of ^{18}F-FDG and its production by cyclotron can become limitations and new needs have arisen in terms of β^+ or γ emitting radioelements.

While increasing interest in radioisotopes such as gallium-68, with short physical periods but produced on site by generators, there is a need for the use of isotopes with longer lifetimes compatible with biological vectors having slower biodistribution kinetics. The positron emitter Zr-89 ($t_{1/2}$ = 78.5 h) or the gamma emitter In-111 ($t_{1/2}$ = 67.9 h) thus appear to be the most suitable. Radio-metals, which can not be injected in their free form, must be used as thermodynamically and kinetically stable complexes. Suitably functionalized tetraazamacrocycles are known to form highly stable complexes with cationic metals. Thus, ions such as Ga(III), In(III) and Zr(IV) having very similar coordination properties such as a high affinity for N- or O-donating ligands, can typically be complexed by macrocycles functionalized by O-coordinating arms.

Recently, in the group, a new family of Zr^{4+} chelates, with four hydroxypyridinone (HOPO) groups pre-organized around a cyclam platform, has already demonstrated its efficiency for Zr-89 radio-labelling. To confirm and to continue this work, the recruited post-doctoral student will continue the synthesis and the study of the coordination properties of new tetraazamacrocyclic ligands functionalized by HOPO groups for the complexation of the 3 metals of interest. The aim will also be to synthesize bifunctional analogues (BCA) in order to introduce a reactive group allowing the addition of both biological vector for cancer imaging and chemical vector for the acquisition of images of the hypoxia's process or the deposition of amyloid plaques.

Modalities. The post-doctoral position will take place at the UMR CNRS 6521 of the University of Brest for 12 months starting the 1st of October.

Funding. The post-doctoral position will be financed by « Maison de la Chimie » with a monthly remuneration of approximately 2000 euros.

Candidate skills. The candidate must have good skills in organic chemistry (synthesis and characterization) and in coordination chemistry (kinetic and thermodynamic studies).

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