Université de Bretagne Occidentale
UMR CNRS 6521 "*Chimie, Electrochimie Moléculaires et Chimie Analytique*"

Post-Doctoral Position in Chemistry
18 months (ANR Funding)

Azamacrocyclic synthesis for new peptide-based radiopharmaceuticals

Laboratoire CEMCA, UMR CNRS 6521
Université de Brest (UBO)
Equipe « Chimie Organique, Santé et Matériaux »
Groupe « Macrocycles Azotés et Coordination »
https://www.umr6521.cnrs.fr/

Abstract of the project

The PanCaIKS (Pan-Cancer Imaging and Killing Strategy) ANR project aims to develop an original **receptor-specific radiolabeled peptide** for bad prognosis tumor imaging and therapy. The radiopeptide, mimicking the C-terminal Binding Domain (CBD) of Thrombospondin-1 (TSP-1) will target the CD47 receptor, overexpressed by cancer cells.
In this project, our task is **to provide bifunctional macrocyclic ligands optimized for the different families of radiometals envisaged**. Despite dota chelator and its derivatives are widely explored for the complexation of radiometals in preclinical studies, in some cases they display a **lack of selectivity which compromises the use of the associated radioelement *in vivo***. **Therefore, the design of radiopharmaceutical tools, for both cancer treatment and imaging, requires expanding i) the repertoire of the chelators** to molecules **not leading to a release of the radioisotope *in vivo*** and ii) **the associated radiometals** (β^- or α emitters for therapy; β^+ or γ emitters for TEP or SPECT, respectively), including "theranostic pairs" whose constitute ideal theranostic tools while requiring the exploration of a unique associated chelator.
In a later stage, the radiopeptide will be evaluated *in vitro* on pan-cancer cell lines. Pancreas and Triple Negative Breast Cancers will be chosen as models for the *in vivo* proof of concept (POC). This is an original approach since this receptor has not been targeted in the field of Peptide Receptor Radionuclide Therapy (PRRT) until now.

Postdoctoral

Position profile: The young researcher, localized in the CEMCA Laboratory (UMR 6521) will have a serious background in organic chemistry (and if possible in macrocyclic chemistry). A good knowledge in bioconjugation reactions (click chemistry, NHS, maleimide…) as well as an expertise in purification by HPLC will also be important additional assets. The post-doc will

also have an affinity for bio-applications and will frequently interact with the different partners of the project.

Researched profile: We are looking for a motivated and experienced candidate in organic synthesis with a strong openness to coordination chemistry and health applications, particularly in imaging / nuclear medicine. A good knowledge in thermodynamic and kinetic studies as well as an expertise in the synthesis and purification of metal complexes by HPLC will be important. The young researcher will also have to explore the structural studies of the complexes and will frequently interact with the other partners including the peptide-conjugated studies. One internship with our collaborator is expected to include peptide conjugation in his/her PhD works and final skills.

References:

- M. Le Fur, M. Beyler, E. Molnár, O. Fougère, D. Esteban-Gómez, G. Tircsó, C. Platas-Iglesias, N. Lepareur, O. Rousseaux, R. Tripier, The role of the capping bond effect on pyclen natY^{3+}/90Y^{3+} chelates: Full control of the regiospecific: N-functionalization makes the difference, *Chem. Commun.*, **2017**, *53*, 9534-9537.
- M. Le Fur, M. Beyler, E. Molnár, O. Fougère, D. Esteban-Gómez, G. Tircsó, C. Platas-Iglesias, N. Lepareur, O. Rousseaux, R. Tripier, Stable and Inert Yttrium(III) Complexes with Pyclen-Based Ligands Bearing Pendant Picolinate Arms: Toward New Pharmaceuticals for β-Radiotherapy, *Inorg. Chem.*, **2018**, *57*, 2051-2063
- G. Nizou, C. Favaretto, Francesca Borgna, P. V. Grundler, Nathalie Saffon-Merceron, C. Platas-Iglesias, O. Fougère, O. Rousseaux, N. P. van der Meulen, C. Müller, M. Beyler, R. Tripier, Expanding the Scope of Pyclen-Picolinate Lanthanide Chelates to Potential Theranostic Applications, *Inorg. Chem.*, **2020**, *59*(16), 11736-11748.

Application before 01/12 /2023:
CV, cover letter and 2 letters of reference must be sent to:

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Starting: January 2024
Salary: ~2600 euros (before taxes)