Cancers Diagnosis by multimodal molecular imaging PET / MRI

Financement :
ARED 50% demanded / CDE 50% acquired (UBO)

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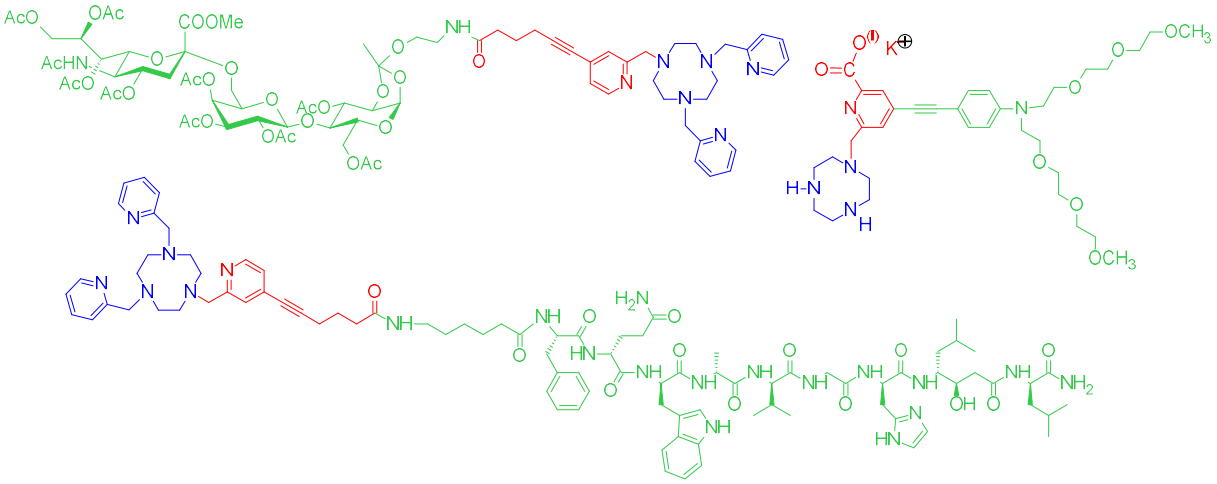
Contexte : Polyazacycloalcanes like 1,4,7-triazacyclononane (tacn) are characterized by their excellent complexing properties for ionic substrates, explaining their involvment in numerous applications. In medicinal research, applications of their metallic complexes are directed towards diagnosis imaging (MRI, PET and Optic Imaging), therapy with radiotherapy or photodynamic therapy (PDT). This wide applications spectrum allows to understand the importance of controling the chemistry of these compounds.
Our group is expert in polyazacycloalcanes chemistry area and has already described derivatives of tacn chelators of Zinc(II) characterized as a MRI sensor for Zn(II) detection and also Copper (II) for PET imaging and radiotherapy applications (respectively with radioisotopes Copper-64 and Copper-67). We are now developing luminescent probes for optic imaging that requires the synthesis of tacn based sophisticated platforms.



Examples of sensors based on tacn synthesized by our group

Issues : Gd^{3+} MRI contrast agents are widely used for clinical MRI examinations. However, they pose a risk to patients with renal impairment (nephrogenic systemic fibrosis). Studies have also shown that repeated injection of these agents can lead to accumulation of Gd^{3+} in tissues and bones. In addition, the use of these Gd^{3+} contrast agents, which are eliminated by the kidneys following the examinations, also causes an estimated release of between 20 and 50 tonnes of gadolinium per year into the environment. It is found in many aquatic environments in abnormally high concentrations, but also in tap water in concentrations that are currently negligible in terms of potential risk to human health. In this context, contrast agents based on Fe^{3+} and Mn^{2+} cations characterised by a spin of 5/2 represent interesting alternatives to Gd^{3+}. The objective of the project is to synthesise new potential MRI contrast agents and new bimodal PET/MRI probes based on these cations.

Mission : The work of the doctoral student recruited will focus on the development of new ligands of interest for the complexation of Fe^{3+} and Mn^{2+}, on their characterisation and the study of their complexing properties (thermodynamic study, kinetics and solid state study) with respect to these metals. Various binding functions of the synthesised ligands will be envisaged, allowing, in the long term, conjugation on various biological materials in order to obtain bimodal probes.

Collaboration :
National collaboration : Centre de Biophysique Moléculaire, CNRS, Orléans, MRI studies
International collaboration/ mobility : Dr Ester Boros, Université de Stony Brooks, USA, PET studies

Profil recherché : The candidate should have a strong background in organic synthesis and if possible in the study of macrocyclic compounds for the complexation of metal cations. An affinity for biological applications in the field of health will be a plus for the successful completion of the projet.

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