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^{89}Zr-labeled radioimmunoconjugates with bispidine ligands

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Context: Recent achievements in the synthesis and coordination chemistry of bispidines (bispidine = 3,7-diazabicyclo[3.3.1]nonane) have paved the way to a new field of application of bispidine coordination complexes: medical imaging and more particularly magnetic resonance imaging (MRI)[1] and positron emission tomography (PET).[2,3] For each of these two techniques, a metal ion (Mn for MRI or a radioisotope for PET) plays the main role of "reporter" and induces the signal. Nevertheless, in both cases, the ions must be chelated and form complexes resistant to *in vivo* dissociation. The particularity of bispidine ligands lies in their rigid and pre-organized skeleton, which allows for fast complexation kinetic in highly dilute conditions suitable for PET and for a strong kinetic inertness of the complexes favourable to their *in vivo* application.

Objective: This project aims at developing bispidine derivatives for the *in vivo* detection of α-synuclein aggregates by PET with 89-Zr. Such aggregates are very promising diagnostic and therapeutic targets for synucleinopathies such as Parkinson and Lewy bodies diseases.[4] We aim at providing a library of new chelates suitable for Zr^{4+} complexation. Their complexation with Zr^{4+} will be characterised by state-of-the art physicochemical techniques (coll. Dr Mourad Elhabiri, CBM/LIMA UMR 7042). The most promising chelates will be conjugated with biomolecules (mAbs, nanobodies) targeted to the synuclein aggregates. Radiolabelling (coll. Dr Frédéric Boisson, IM/UMR7178) and preliminary *in vitro* and *in vivo* imaging will be explored on murine models with diffuse synuclein aggregates and cognitive deficiency (coll. Dr Laurette Boutillier, LNCA).

Expected skills: Multi-stage organic synthesis and standard characterization techniques (NMR, IR, mass spectrometry); Skills and a taste for coordination and physical chemistry; Control of bibliographical research tools; English; Energy, rigour, method and tenacity.

Application/further information: Just contact me at aline.nonat@unistra.fr (before June 15th, 2021).

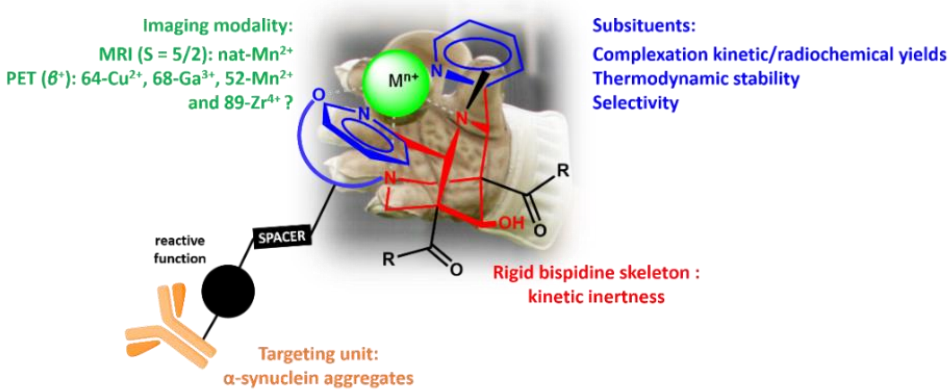

Fig. 1. Bispidine chelators for synuclein imaging: a compromise between fast complexation and strong kinetic inertia.

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