GADOLINIUM COMPLEXES FOR ZINC DETECTION BY MAGNETIC RESONANCE IMAGING: FROM RATIONAL DESIGN TO IN VIVO APPLICATIONS

Célia Bonnet[1]

[1] *Centre de Biophysique Moléculaire CNRS, Université d'Orléans, Rue Charles Sadron, 45071 Orléans Cedex 2, France*

Magnetic Resonance Imaging (MRI) has been devoted for a long time to obtaining anatomical and functional images. Recently emerging applications in molecular imaging seek information at the molecular level, looking at the biochemical or physiological abnormalities underlying the disease. Unlike anatomic imaging, molecular imaging always requires an imaging probe that is selectively responsive to the parameter to detect. Gd^{3+}-based contrast agents are particularly well-adapted for this purpose and most often the changes on the efficacy (relaxivity) are based on changes of the hydration number and/or rotational dynamics of the complexes; these two parameters being the easiest to be tailored by the chemist.

Zinc is the second most abundant transition metal ion in humans, and it plays a central role in controlling gene transcription and metalloenzyme function. However, its quantitative distribution and its exact role are not well understood. It has also been shown that disturbances in Zn^{2+} homeostasis is implicated in neurodegenerative diseases (Alzheimer, Parkinson), diabetes, and cancers (prostate, pancreas and breast).[1] Therefore, monitoring Zn^{2+} *in vivo* by non-invasive technique such as MRI is important in biomedical research to understand its biological role, and to provide earlier diagnosis for specific pathologies.[2]

We will present the rational development of small molecular zinc responsive contrast agents based on a pyridine unit already used for Gd^{3+} complexation,[3] to which a zinc complexing unit has been added through a linker (Figure 1A),[4] as well as bioinspired systems based on the zinc finger peptide (Figure 1B).[5] Challenges in terms of selectivity, and quantification[6] will be discussed, as well as our last in vivo results.[7]

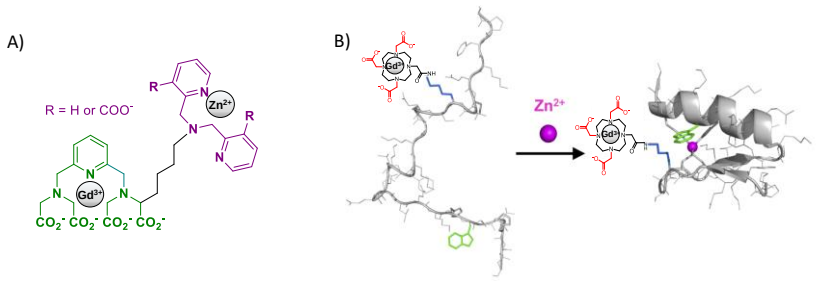

Fig. 1 A) Structure of the molecular Zn-responsive MRI contrast agents; B) Principle of Zn detection with the zinc finger peptide

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