Post-doctoral position for one year from October 2020

Centre de Biophysique Moléculaire
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Development of MRI contrast agents for selective detection of physiological cations

Metal ions, such as zinc and copper, play a fundamental role in living systems as they are involved in many essential biological processes. Their concentration is highly regulated by the cells and disruption of their homeostasis has been implicated in numerous diseases such as neurodegenerative diseases, cancers, or diabetes. Visualisation of these metal ions in vivo and in real time would enable a better understanding of their role and biodistribution, and early diagnosis of diseases. Due to its excellent spatial and temporal resolution and non-invasive character, Magnetic Resonance imaging (MRI) is a choice technique. The low sensitivity of MRI can be compensated by the introduction of a contrast agent, which can be specific of a given biomarker. These contrast agents are mostly Gd^{3+} or Mn^{2+} complexes. The efficacy (relaxivity) of the contrast agent must be modulated by the complexation of the cation to detect, mostly through a change in the coordination sphere of Gd^{3+} or Mn^{2+} or a global change in the size of the complex. We have recently developed a family of contrast agents responsive to Zn^{2+} through an interaction with human serum albumin (HSA). However, the selectivity for a given cation, and even for a given oxidation state is crucial but can be difficult to obtain, particularly for Cu^{2+} vs Zn^{2+} and vice versa can be difficult to obtain. We propose to develop innovative methods based on ParaCEST probes (Paramagnetic Chemical Exchange Saturation Transfer). These are paramagnetic complexes (in particular Ln^{3+} complexes) bearing paramagnetically shifted exchangeable protons. Cation detection can be achieved by modulation of the exchange rate and/or the resonance frequency of the mobile protons.

The postdoctoral researcher will be in charge of the synthesis of macrocyclic ligands and will study the corresponding Ln^{3+} complexes and their response to physiological cations by various methods such as NMR, potentiometry, UV-visible spectroscopy…

The candidate should be an expert in organic synthesis. An experience in coordination chemistry and physical chemistry will be an asset. He/she will be highly motivated and eager to work in a multidisciplinary environment and at the interface between chemistry and biology.

To apply, send a CV, a summary of your research activity, a cover letter and two references and/or support letters to celia.bonnet@cnrs.fr

Deadline for application: 1st of July 2020