Ph.D. in Molecular Chemistry
at Univ. Grenoble Alpes (Grenoble, France)

Carbazole-based luminescent lanthanide bioprobes for reactive oxygen species sensing in live cells

Host laboratories: LCBM (Lab. Chimie et Biologie des Métaux) and CIRE (Chimie Inorganique Redox)

Project description: The context of this Ph.D. project is luminescence imaging, and more specifically biphotonic confocal microscopy imaging. Lanthanide(III) complexes have fantastic luminescent properties that make them very attractive for bioimaging. Classic lanthanide-based luminescent bioprobes require high energy excitation by UV-visible light (300-450 nm), which is absorbed and scattered by the biological tissues and causes photodamage. Indeed, for biological imaging applications, working with both excitation and emission in the biological transparency window (600-1500 nm) is preferred to avoid these problems. This can be achieved by using Europium(III) as a red emitter and a light-harvesting antenna (to sensitize Eu^{3+} luminescence) that presents two-photon absorption properties. During the past two years, we have developed a Eu^{3+} complex featuring a carbazole antenna that features interesting two-photon absorption properties. This complex was conjugated to a cell penetrating peptide, allowing its delivery to the cytosol. This system was successfully used for two-photon imaging of live cells. Now, our goal is to improve it and to develop responsive probes based on this first imaging agent. The first objective of this Ph.D. will be to optimize the luminescence properties of this Eu^{3+} complex by tuning the photophysical properties of the carbazole antenna. Indeed, to improve its luminescence properties, we need to suppress an unproductive photoinduced electron transfer between the carbazole antenna and Eu^{3+}. This will be done by introducing substituents on the carbazole unit. The second objective is to perform organelle addressing in cells. The parent complex was successfully delivered into the cytosol of live cells but the next challenge is now to address it to a chosen organelle (e.g. nucleus, endoplasmic reticulum, mitochondria). This will be done by appending a localization signal peptide to the complex. The third objective will be to design a redox-active probe able to detect either specific radical reactive oxygen species, or more generally, cellular redox potential. This will be achieved by appending a redox active radical or pro-radical unit (nitroxide or hydroxylamine) to the Eu^{3+} complex. Europium luminescence will be switch ON or OFF depending on the redox status of the redox-active pendant. All the new luminescent systems will be characterized in vitro and evaluated for two-photon confocal microscopy imaging of live cells. This project will lead new performant and unprecedented Eu^{3+}-based two-photon imaging agents.

Student role: The Ph.D. fellow will be required to perform the synthesis of the Eu^{3+} complex/peptide conjugates (organic and peptide synthesis), their spectroscopic, physicochemical and electrochemical characterizations and microscopy on live cells. The Ph.D. fellow will be trained in these techniques and will be responsible for each part of the project.

Required skills: Master degree in molecular (organic, bioorganic or bioinorganic) chemistry. A strong background in organic synthesis is mandatory. Knowledge in peptide synthesis, and/or luminescence spectroscopy will be appreciated.

Contact: send CV and motivation letter, recommendation letters and Master grade transcripts to

- Olivier SENEQUE: olivier.seneque@cea.fr (LCBM)
- Jennifer K. MOLLOY: jennifer.molloy@univ-grenoble-alpes.fr (CIRE)

Deadline: 11th March 2022