FrenchBIC Webinar

Replacing boron atom by a metal ion in aza-BODIPY fluorophores: a new way to design innovative imaging probes

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Aza-boron-dipyrromethenes (aza-BODIPYs) have gone from being a scientific curiosity to a class of fluorophores of major interest just like rhodamines or cyanines. These *N*-analogues of BODIPYs have built their reputation thanks to their ease of synthesis, their high stability, their good quantum yields, and because they absorb and emit light in the NIR-I (700-900 nm, wavelengths sought after for *in vivo* optical fluorescence imaging or even for surgical assistance).

Some aza-BODIPYs, that we have developed,[1] can even emit in the NIR-II (1000-1700 nm), which allows to further improve the resolution of the images. This area is much more difficult to access and many works have been undertaken to try to reach this area by modifying the substituents of the aza-BODIPYs, by rigidifying them, by extending their conjugated system, but very few groups have focused their attention on the boron atom of the aza-BODIPY core. Indeed, this fluorophore can be considered as an aza-dipyrromethane ligand chelating a boron atom, which rigidifies this structure. We can wonder what would happen if this boron atom is replaced by a metal.

To investigate the impact of the metal on the photophysical properties of the aza-MetalDIPY (azaMDIPY) complexes, we studied the chelation of elements from group 13[2] as well as group 4. A focus will be done on the Ga-derivative, that have been water-solubilized and turned to a bimodal probe (NIR-fluorescence/TEP). Especially, a NIR-I/NIR-II imaging study of its biodistribution in subcutaneous tumor bearing mice (U87MG, IGROV1, and A375), its potential for fluorescence-guided surgery, its radiolabelling, and the bimodal PET/NIR study of [^{68}Ga]-azaGaDIPY in orthotopic brain tumor bearing mice (U87MG) will be presented.

[1] Godard *et al*. *Bioconjugate Chem.* **2020**, 31(4), 1088-1092. https://doi.org/10.1021/acs.bioconjchem.0c00175

[2] Godard *et al*. *Inorg. Chem.*, **2023**, 62 (13), 5067-5080. https://doi.org/10.1021/acs.inorgchem.2c03918