X-ray Sensitive Micellar Transporters for Controlled Drug Release Assisted by MRI

Melisa Esther Gonzalez[1], Thomas Vangijzegem[1], Dimitri Stanicki[1] and Sophie Laurent[1,2]

[1]General, Organic and Biomedical Chemistry Unit, NMR and Molecular Imaging Laboratory, University of Mons (UMONS), 7000 Mons, Belgium.
[2]Center for Microscopy and Molecular Imaging (CMMI), 6041 Gosselies, Belgium.

Current cancer therapies are limited by imprecise drug targeting and systemic side effects. This project aims to develop a novel drug delivery system based on self-assembled micellar nanocarriers activated by ionizing radiation (IR) and monitored using Magnetic Resonance Imaging (MRI), enabling precise drug release control.

Our approach centers on an amphiphilic molecule combining a light-sensitive azobenzene moiety with an IR-sensitive gadolinium (Gd) chelate (Figure **1**). This amphiphilic molecule, referred to as Azo-DOTA, has the ability to self-assemble into micelles, forming stable, biocompatible carriers suitable for deep tissue therapy and functioning as MRI contrast agents [1,2]. High atomic number metals like Gd absorb high-energy photons, releasing secondary electrons that could trigger azobenzene isomerization. In this process, trans-Azo-DOTA self-assembles into micelles, while its isomerization into cis-Azo-DOTA could lead to micelle disruption and controlled drug release.

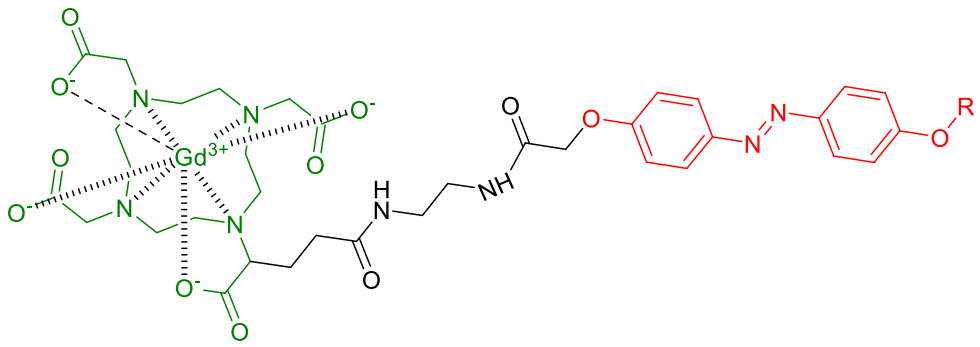

Figure **1**. Illustration of the amphiphilic molecule containing (i) an IR-sensitive Gd chelate (green), (ii) an azobenzene photoswitch (red) and (iii) variable hydrophobic chains (R).

In this project, we will synthesize structural analogues of the Azo-DOTA molecule, by modifying their structure to enhance drug-loading capacity and IR-responsive drug release. Micelle formation, stability, and properties will be characterized using Dynamic Light Scattering (DLS) and Transmission Electron Microscopy (TEM). Chemotherapeutic drugs will be encapsulated, and controlled release under UV light and X-ray irradiation will be evaluated to assess the stimuli-responsive mechanism. *In vitro* tests on cancer cell lines will assess cytotoxicity and IR-triggered release efficacy.

This study anticipates developing stable, biocompatible micellar systems with enhanced drug-loading capacity and MRI contrast properties. Controlled drug release via IR exposure is expected, supporting synergistic effects between radiotherapy and chemotherapy, reducing radiation doses and systemic toxicity. These results could advance cancer theranostics with precise, real-time monitored drug delivery.

References

[1] A. Guesdon-Vennerie, P. Couvreur, F. Ali *et al*. *Nat Commun*, **2022**, 13, 4102.
[2] Y. Heta, K. Kumaki, H. Hifumi, *et al. Photochemistry and Photobiology*., **2012**, 88, 876–883.