Development of multimodal platforms for photodynamic therapy

Figliola, C. and Ulrich, G.  

Institut de Chimie et Procédés pour l'Energie, l’Environnement et la Santé (UMR 7515)  
25 rue Becquerel, 67087 Strasbourg Cedex 2, France  
(figliola@unistra.fr)

ABSTRACT:

Photodynamic therapy (PDT) is a medical treatment using the light in combination with a photosensitizer (PS) and molecular oxygen (O\(_2\)) against cancers and microbial infections.\(^1,2\) The therapeutic effects of PDT derive from the absorption of the light by the PS, which reacts with O\(_2\) and produces singlet oxygen (O\(_2\)) and other reactive oxygen species (ROS) causing cell death, vessel damage and an inflammatory and immune response.\(^1,2\) Nowadays, although its minimal systematic invasiveness and toxicity, PDT is used as complementary to other established therapeutic solutions, such as radiotherapy, chemotherapy or surgery.\(^3\) Our laboratory proposes the optimization of PDT-based therapeutic protocols by developing multimodal platforms including a two−photon absorption PS for PDT,\(^4\) a one−photon absorption near-infrared (NIR) fluorophore for imaging and a targeting molecule, which has a high affinity for a specific biomarker of the chosen pathological condition. The selectivity of systems will be also obtained by the ability of PS to generate O\(_2\) only into the targeted cells via stimuli-responsive reactions.\(^7\) These systems will be accomplished in three parts. First, new difluoroboron pyridine-based complexes\(^5\) and pyrrolyldipyrrins\(^6\) scaffolds will be studied as potential PS. Secondly, the synthesis of theranostic dyads will be shown using the previously developed PS and NIR BODIPY-inspired fluorophores. Unlike the photosensitizing moiety, the fluorophores will be always active allowing the real-time visualization of the system towards its biodistribution, accumulation into the targeted tissues, body clearance, the PS-light administration interval and the light dose.\(^8\) Last, investigation of potential organic platforms and optimization of the synthetic strategies to link covalently the PS, the NIR fluorophore and the targeting molecule will be presented.

Figure 1 : Current research: development of multimodal organic platforms connecting a stimuli-responsive 2PA PS, a NIR imaging agent and a disease-targeting molecule.

References