

Development of multimodal platforms for photodynamic therapy

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ABSTRACT:

Photodynamic therapy (PDT) is a medical treatment using the light in combination with a photosensitizer (PS) and molecular oxygen ($^3\text{O}_2$) 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 $^3\text{O}_2$ and produces singlet oxygen ($^1\text{O}_2$) 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 $^1\text{O}_2$ only into the targeted cells via stimuli-responsive reactions.⁷ These systems will be accomplished in three parts. First, new difluoroboron pyridine-based complexes⁵ and pyrrolyldipyrins⁶ 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.

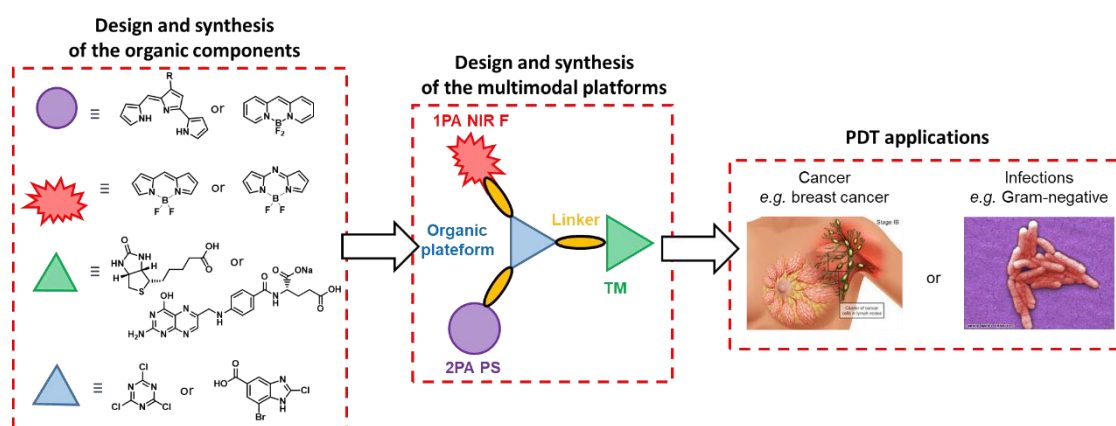


Figure 1 : Current research: development of multimodal organic platforms connecting a stimuli-responsive 2PA PS, a NIR imaging agent and a disease-targeting molecule.

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