PhotOnline'2023
Web-conference organized by and for young researchers – 2nd edition

A novel molecular dyad for combined PDT and NO-PDT in cancer cells

Cristina Parisi[1*], Giuseppe Longobardi[2], Adriana C.E. Graziano[1], Aurore Fraix[1], Claudia Conte[2], Fabiana Quaglia[2] e Salvatore Sortino[1].

([1]*Department of Drug and Health Sciences, Laboratory of Photochemistry, University of Catania, Unict, Catania, Italy*
[2]*Department of Pharmacy, Drug Delivery Laboratory, University of Napoli Federico II, Unina, Napoli, Italy*
[*]*cristina.parisi@phd.unict.it*

Keywords: Photodynamic therapy, Nitric oxide, Light, Multimodal therapy, Polymer nanoparticles

Photodynamic therapy (PDT) is a well-known therapeutic modality based on the photocontrolled generation of the highly reactive singlet oxygen ($^1O_2$) for the treatment of malignant lesions like cancer[1]. Combination of PDT with other unconventional therapeutic species is emerging as a promising strategy which aims at exploiting the additive/synergistic effects arising from multiple species in order to increase the effectiveness of therapeutic treatment and to minimize side effects[2]. On this regard, the coupling of PDT photosensitizers (PSs) with nitric oxide photodonors (NOPDs) is opening new perspective. Molecular dyads integrating within the same molecular skeleton PSs and NOPDs are of great interest because offer the advantage to photorelease $^1O_2$ and NO in the "same region of space". However, the design of such systems is a difficult task since the generation of comparable amounts of $^1O_2$ and NO is necessary in order to observe the desired improved photodynamic effects but $^1O_2$ quantum yields (Φ_Δ) of many PSs are often much larger than those of NO (Φ_{NO}) of organic NOPDs[2]. Herein we present the design, photochemical properties and biological evaluation of a novel molecular dyad integrating a PS and a NOPD within the same skeleton (Figure 1) and generating, under activation with visible light, $^1O_2$ and NO with comparable quantum yields[3]. Besides, the non-fluorescent NOPD unit becomes highly fluorescent after the NO release, acting as an optical reporter for the NO photogenerated. The dyad is not soluble in water but is effectively entrapped in water-dispersible, biodegradable polymeric NPs made of mPEG-PCL. The NPs effectively deliver the dyad into the cytoplasm of HepG2 hepatocellular carcinoma cells. A remarkable decrease of cell viability is observed for the loaded NPs using very low concentrations of the dyad and very low light doses, as result of the combined photodynamic action of $^1O_2$ and NO. These properties make this dyad a very appealing candidate for further biomedical studies.

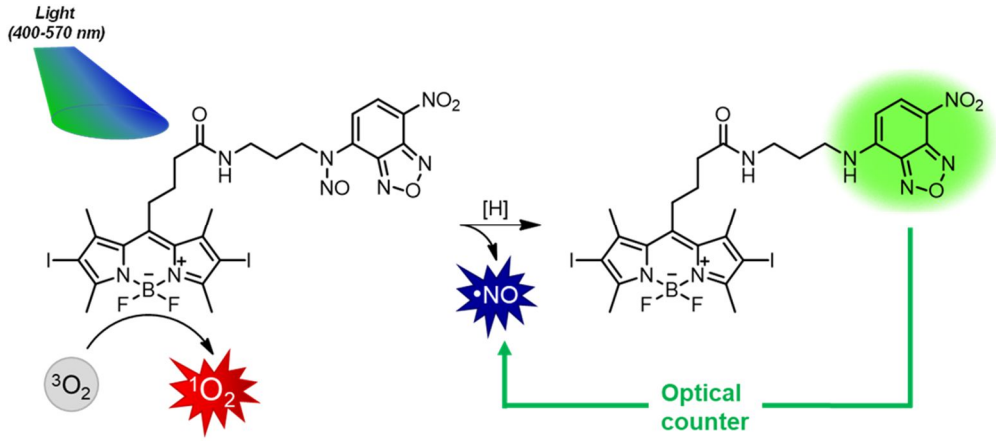

Figure 1. Structure of the molecular dyad photogenerating $^1O_2$, NO and a stable photoproduct under visible light.

[1] M. R. Hamblin, T. Hasan, Photochemical and Photobiological Sciences, **2004**, 3, 436-450.
[2] A. Fraix, S. Sortino, Photochemical and Photobiological Sciences, **2018**, 17, 1709-1727.
[3] C. Parisi, G. Longobardi, A.C.E. Graziano, A. Fraix, C. Conte, F. Quaglia, S.Sortino, Bioorganic Chemistry, **2022**, 128, 106050.