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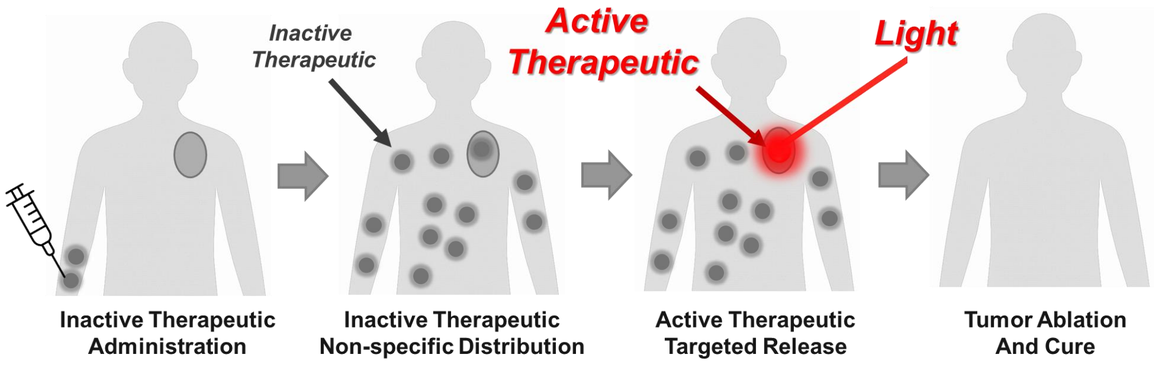
A Novel Supramolecular Approach for Red-Light-Photosensitized Nitric Oxide Release

C. Parisi [1], **F. Laneri** [1], **G. Longobardi** [2], **A. Fraix** [1], **C. Conte** [2], **A. Pastore** [3], **M. Stornaiuolo** [3], **A.C.E. Graziano** [1], **M. Seggio**[1], **O. Catanzano** [4], **F. Quaglia** [2,*], **S. Sortino** [1,*]

[1] Laboratory of Photochemistry, Department of Drug and Health Sciences, University of Catania, Catania, Italy
[2] Drug Delivery Laboratory, Department of Pharmacy, University of Napoli Federico II, Napoli, Italy
[3] Department of Pharmacy, University of Napoli Federico II, Napoli, Italy
[4] Institute for Polymers, Composites and Biomaterials (IPCB-CNR), Pozzuoli (NA), Italy

INTRODUCTION & AIM

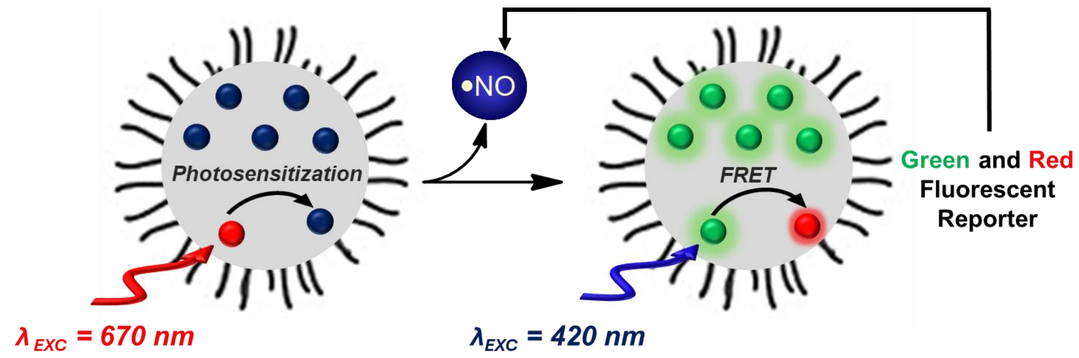
The low approval rate of new chemotherapeutics and the rise of Multi Drug Resistance (MDR) call for the pursuit of "unconventional" therapeutic strategies against cancer. In this context, photopharmacology emerges as an innovative approach, enabling more precise and safer treatments: light-activatable drugs remain inactive and non-toxic in the body, and only generate cytotoxic species upon localized irradiation [1].



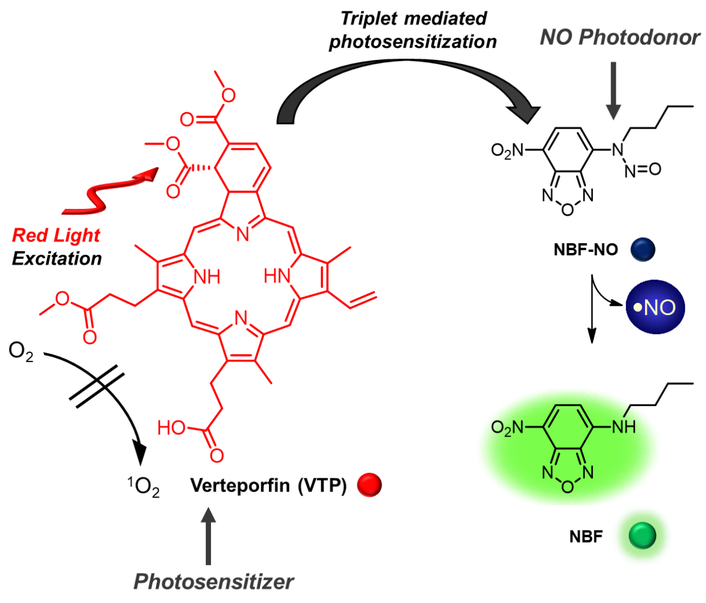
Among the most promising candidates is nitric oxide (NO), a multitarget molecule unaffected by MDR. Due to its short lifetime, NO acts only near its site of production, limiting the systemic toxicity typical of many conventional Drugs [2]. However, its effects strongly depend on concentration and localization, requiring precise spatiotemporal control. Light-triggered release from suitable NO photodonors (NOPDs) represents an optimal strategy, highlighting the need to develop materials capable of releasing NO within the therapeutic window [3,4].

AIM OF THE WORK

PROPOSED STRATEGY



NO RELEASE MECHANISM



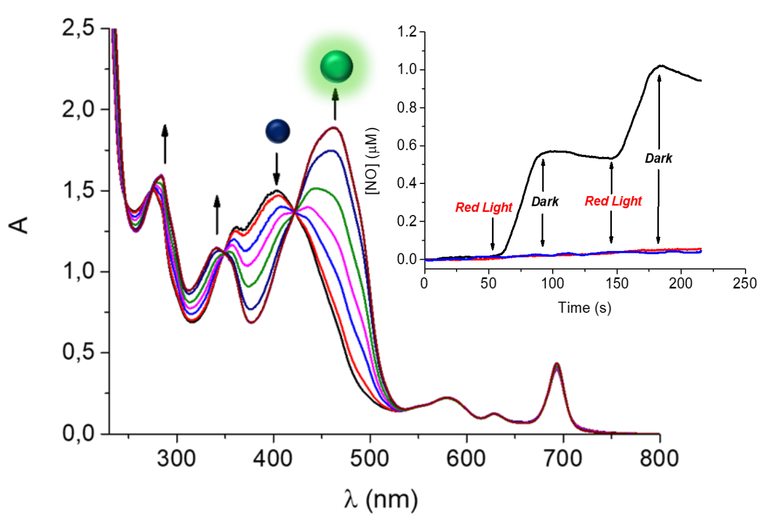
AIM OF THE WORK:

Demonstrate red-light triggered NO release from a blue-light activatable, self-reporting NOPDs via supramolecular photosensitization.

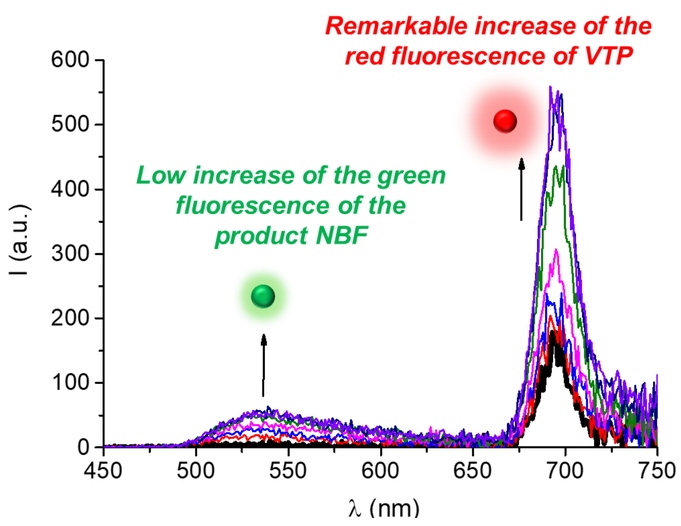
RESULTS & DISCUSSION

PHOTOCHEMICAL CHARACTERIZATION

DIRECT AND INDIRECT NO DETECTION



SELF-REPORTING FLUORESCENCE



BIOLOGICAL VALIDATION OF THE NANOMEDICINE

EVOLUTION OF GREEN FLUORESCENCE IN CANCER CELLS

CELLULAR VIABILITY

CELLULAR UPTAKE

EXTENSIBLE STRATEGY:

The proposed strategy is inherently versatile and can be extended to a wide range of polymers and photosensitizers, paving the way for broader applications of red-light triggered NO release.

CONCLUSION

This work demonstrates a supramolecular photosensitization strategy that enables catalytic NO release from a blue-light activatable NOPD using biocompatible red light, with a ~300 nm shift toward longer excitation wavelengths. The process generates a stable green fluorescent photoproduct that serves as a real-time optical reporter. Importantly, the strategy requires no chemical modification of the NOPD or sophisticated excitation sources, offering a versatile platform with strong potential for future bio-applications.

REFERENCES

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[2] Parisi C., Laneri F., Fraix A., Sortino S. *J. Med. Chem.* **2024**, *67*, 16932–16950.
[3] Fraix A., Parisi C., Longobardi G., Conte C., Pastore A., Stornaiuolo M., Graziano A.C.E., Alberto M.E., Francés-Monerris A., Quaglia F., Sortino S. *Biomacromolecules,* **2023**, *24*, 3887–3897.
[4] Laneri F., Parisi C., Seggio M., Fraix A., Longobardi G., Catanzano O., Quaglia F., Sortino S. *J. Mater. Chem. B*, **2024**, *12*, 6500-6508.