XXXVI Congress

of the Italian Association of Photobiology

PROGRAMME AND BOOK OF ABSTRACTS



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Società Italiana di Fotobiologia

22-24 June 2026

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Monday, 22 June	Tuesday, 23 June	Wednesday, 24 June
13:00-19:30	**09:00-18:15**	**09:15-13:30**
Session 1 Opening Scientific Session	**Session 3** Photodynamic Therapy in Cancer Microenvironments	**Session 6** Photosensitizer Design and Photodynamic Strategies
Session 2 Photosynthesis and Biohybrid Systems	**Session 4** Advanced Photosensitizers and Combination PDT Strategies	**Session 7** From Photo-immuno-modulation to One Health Applications
SIFB General Assembly	**Session 5** Photodermatology: From Therapy to Imaging	**Closing Session**
	Young Investigator Award Ceremony	
	<u>Social Dinner – 20:30</u> ***Osteria "L'Oste Sobrio"*** **Via Cesare Beccaria, 6**	

Invited lectures	Oral presentations	Young Investigator Award
30 min + 5 min discussion	20 min + 3 min discussion	20 min + 5 min discussion

Monday, 22 June 2026

13:00	**Registration**	
14:00-14:30	**Congress Opening, Welcome Remarks**	
Time	**Speaker / Activity**	**Title**
SESSION 1 – Opening Scientific Session		
CHAIR: Carlo Matera		
14:30-15:05	**Laia Josa-Culleré**	**Photoswitches and photocages to eliminate cancer stem cells under external light control**
15:05-15:25	Ramona Santini ***Frontiers Fellowship***	Targeted covalent photoswitch for two-photon control of endogenous receptors
15:25-15:45	Giorgia Miolo	Photostability of therapeutic mAbs and ADCs under real-life light doses
15:45-16:10	**Coffee break**	
SESSION 2 – Photosynthesis and Biohybrid Systems		
CHAIRS: Maya D. Lambreva, Francesco Milano		
16:15-16:50	**Lorenzo Ferroni**	**Distinctive morpho-functional adaptations for photosynthesis in deep shade in the ancient vascular plant genus *Selaginella* (Lycopodiophyta)**
16:50-17:10	Stefano Santabarbara	Evidence of bidirectional electron transfer in far-red light adapted Photosystem I
17:10-17:30	Francesco Milano	In-field tomato growth under blue-depleted sunlight from a semi-transparent perovskite panel
17:30-17:50	Maya D. Lambreva	Tiny diamonds, stronger cells: hydroxy-lated nanodiamonds mitigate oxidative stress in *Chlamydomonas reinhardtii*
17:50-18:10	Rossella Labarile	Chromatophore-based biohybrid archi-tectures for solar-pumped laser systems: role of scattering in optical characterization
18:20-19:30	**SIFB General Assembly**	

Tuesday, 23 June 2026

Time	Speaker / Activity	Title
SESSION 3 - Photodynamic Therapy in Cancer Microenvironments		
CHAIR: Giorgia Miolo		
09:00-09:35	Valentina Rapozzi	Nitric Oxide, Nrf2 Signaling and Tumor Hypoxia: Interconnected Determinants of Resistance and Response in Photodynamic Therapy
09:35-09:55	Thenesia Govender	Development of Multimodal, Light-Activated NO-Based Conjugates for Triple-Negative Breast Cancer Treatment
09:55-10:15	Erna Tintor	CAIX-Targeted Inhibitor-Photosensitizer Conjugates for Enhanced Photodynamic Efficacy Under Hypoxic Tumor Conditions in Triple-Negative Breast Cancer Cells
10:15-10:35	Cosmin Butnarasu	Lighting up mucins: development of polymethine dyes for mucin-responsive sensing in pancreatic cancer
10:35-10:55	Federica Randisi ***SIFB fellowship***	BODIPY-loaded liposomes enhance cellular uptake and PDT efficacy in 2D and 3D models
10:55-11:20	**Coffee break**	
SESSION 4 – Advanced Photosensitizers and Combination PDT Strategies		
CHAIR: Sonja Visentin		
11:20-11:40	Francesca Bianco ***SIFB fellowship***	Orai1 inhibition and PDT: novel combination therapy for Pancreatic Ductal Adenocarcinoma
11:40-12:00	Sara Cascone	Development of Anionized Albumin Formulations for Macrophage-Selective Photoimmunotherapy
12:00-12:20	Melisa Ciglaric	Synthesis of cationic AB_3 *meso*-(4-(*N*,*N*-diethylamino)phenyl)porphyrins for *in vitro* studies on melanoma cells

Time	Speaker / Activity	Title
12:20-12:40	Giulia Giugliano	Machine learning-driven discovery of novel photosensitizers for photodynamic therapy
12:40-13:00	Martina Mušković Lukić	Impact of melanin pigment and hypoxic conditions on (photo)cytotoxicity of amphiphilic *N*-methylated tripyridinium-porphyrins with alkyl chains of different length on melanoma cell lines
13:00-14:30	**Lunch**	
SESSION 5 – Photodermatology: From Therapy to Imaging		
CHAIR: Marina Venturini		
14:40-15:15	Piergiacomo Calzavara Pinton	A lifetime in science: reflections on light based therapies and dermatological research
15:15-15:35	Isacco Cattaneo	Real-life experience from a tertiary phototherapy center on solar urticaria: clinical features, management, and long-term outcomes from a twenty-year cohort
15:35-15:55	Mariateresa Rossi	Photoprotection in Inflammary Dermatoses
15:55-16:15	Gaia Maridati	Frontiers in Photobiology
16:15-16:40	**Coffee break**	
16:40-17:15	Luigi Spiazzi	Physics in photodermatology: quantitative imaging and AI
17:15-17:25	Alessandro Franzini	Light and Edema: An Unexpected Association
17:25-17:45	Marina Venturini	Photodynamic Therapy with Topical Zinc Phthalocyanine RLP068/Cl for Moderate-to-Severe Papulopustular Acne: A Pilot Study
17:45-18:15	Alessio Colleoni ***Young Investigator Award Ceremony***	Photoswitchable Glycomimetics Enable Precision Targeting of LecB in *Pseudomonas aeruginosa*
20:30	**Social dinner Osteria "L'oste sobrio"**	

Wednesday, 24 June 2026

Time	Speaker / Activity	Title
SESSION 6 – Photosensitizer Design and Photodynamic Strategies		
CHAIR: Enrico Caruso		
09:15-09:50	Mathias O. Senge	Molecular and Formulation Strategies for Photosensitizer Design
09:50-10:10	Nika Skokic	Impact of Zn(II) and Cu(II) chelation with methylated tetrakis pyridinium-3-yl porphyrin on antimicrobial properties and photodynamic inactivation
10:10-10:30	Nataliia Emashova	Infrared light-based antimicrobial approach
10:30-10:50	Chiara Di Donato ***SIFB Fellowship***	Phage Platforms for Targeted Antimicrobial Photodynamic Therapy
10:50-11:10	Giuseppe Nocito ***SIFB Fellowship***	A photo-antimicrobial hydrogel based on a tetracationic porphyrin and Captisol® assemblies for wound management
11:10-11:30	**Coffee break**	
SESSION 7 – From Photoimmunomodulation to One Health Applications		
CHAIR: Mariateresa Rossi		
11:30-11:50	Marialaura Giannaccari	Green-Synthesized Prussian Blue Nanoparticles for Synergistic Breast Cancer Therapy
11:50-12:10	Emanuela Peluso	Multilayer of Prussian Blue Nanoparticles with Photothermal Antibacterial Effect
12:10-12:30	Giovanni Romano	Unify, Align, and Educate: Promoting Photodynamic Inactivation within the One Health Framework by COST Action CA24127 PanEuCOPTion
12:30-13:05	Serena Lembo	Light and skin: photoimmunomodulation
13:10	**Closing remarks**	

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Laia Josa-Culleré

Photoswitches and photocages to eliminate cancer stem cells under external light control

L. Josa-Culleré

Institute for Advanced Chemistry of Catalonia (IQAC-CSIC), Jordi Girona 18-26, 08034, Barcelona, Spain

Achieving a localised effect of chemotherapy confined to the tumour site remains one of the major challenges in cancer treatment. Despite significant advances in targeted and precision medicine, many drugs still lack the ability to discriminate between malignant and healthy cells, resulting in narrow therapeutic windows and systemic toxicity. Therefore, novel therapeutic approaches that direct drugs specifically to the tumour area are needed. Another major challenge is the elimination of cancer stem cells (CSCs). Although they represent a minority within the tumour, CSCs play a key role in patient relapse – they are resistant to standard chemotherapy and capable of regenerating the tumour. Due to their close resemblance to healthy stem cells, selective treatments targeting CSCs remain scarce.

In this context, photopharmacology emerges as a promising solution.[1] It is based on using light to modulate the biological activity of drugs with high precision, employing two possible designs: photoswitches and photocages. In recent years, we have demonstrated that light-activated compounds can selectively eliminate both cancer cells and CSCs with spatiotemporal resolution. Our work includes the development of histone deacetylase (HDAC) inhibitors based on azobenzenes[2] and hemithioindigos,[3] some of which inhibit the enzyme and decrease cancer cell viability only under illumination. We have also performed structural optimisation to enable activation with longer-wavelength visible light. Furthermore, we have designed a caged autophagy inhibitor capable of disrupting the formation of CSC spheres upon illumination, and we have proven that it can be activated in an orthotopic tumour in vivo.[4] I will use these case studies to illustrate the design, synthesis, and biological evaluation of light-responsive molecules, highlighting both the opportunities and challenges of this emerging field.

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Ramona Santini

Targeted covalent photoswitch for two-photon control of endogenous receptors

S. Ramona[1,2,3,+], G. Maleeva[1,2,+], R. Sortino[1,2], S. Pons-Allés[1,4], C. Ramos-Guerra[1], C. Matera[1,2,5], P. Gorostiza[1,2,6]

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The study of intact cells and their signaling circuits with light requires a stimulation strategy that is focused, deeply penetrating, and that does not damage them. Implanted optic fibers, light emitting diodes, and luminescent materials operated externally with tissue-penetrating infrared (IR) light are invasive or limited by light attenuation around the illumination point.

To overcome these barriers, two-photon pharmacology takes advantage of femtosecond-pulsed IR laser light to produce deep and spatiotemporally precise cellular stimulation using specially designed photoswitchable drugs. Compounds that can be covalently tethered to the target neuroreceptor perform particularly well. However, the tethered photoswitches reported to date require mutagenesis of the target protein, which prevents using photopharmacology to stimulate the nervous system in wildtype animals. Here, we report the first two-photon optimized targeted covalent photoswitch (TCP_{2P}) that combines the efficient two-photon isomerization of *ortho* fluoro substituted azobenzene with the ability to conjugate to nucleophilic residues of endogenous proteins (AMPA and kainate ionotropic glutamate receptors in neurons). TCP_{2P} is readily obtained by click coupling of two precursor compounds prior to use and after simple incubation it enables controlling neuronal activity at one and two-photon excitation up to 800 nm without genetic modifications.

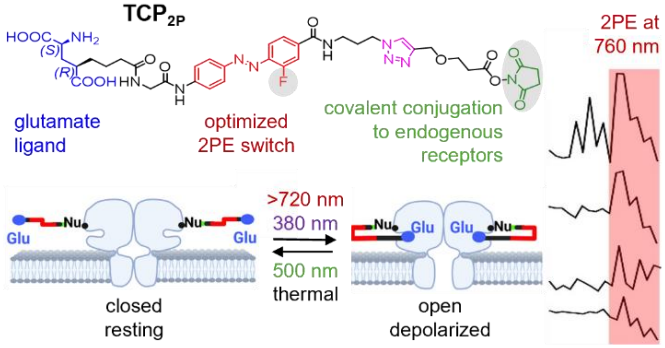


Fig 1. Purpose and design of two-photon optimized targeted covalent photoswitch TCP_{2P}. Top) Chemical structure of TCP_{2P}. Bottom) Activation and channel opening of iGluRs mediated by *trans* and *cis* TCP_{2P} (closed and open ion channel, respectively. Right) Traces of calcium-dependent fluorescence intensity in cultured hippocampal neurons before and during 2P excitation of TCP_{2P} at 760 nm.

This abstract is adapted from:
Santini, R.; Maleeva, G.; Sortino, R.; Pons-Allés, S.; Ramos-Guerra, C.; Matera, C.; Gorostiza, P. Targeted Covalent Photoswitch for Two-Photon Control of Endogenous Receptors. *J. Am. Chem. Soc.* **2026**. https://doi.org/10.1021/jacs.5c19954.

Giorgia Miolo

Photostability of therapeutic mAbs and ADCs under real-life light doses

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Monoclonal antibodies (mAbs) and antibody–drug conjugates (ADCs) represent a rapidly expanding class of biopharmaceuticals that have revolutionised cancer therapy due to their high specificity and reduced toxicity compared with conventional chemotherapies. However, these molecules are inherently susceptible to chemical and physical instability, which may compromise their efficacy and safety throughout their real-life lifecycle.
This study aimed to evaluate the physicochemical stability and biological activity of selected mAbs and ADCs following exposure to light doses mimicking real-life conditions during preparation and administration. The mechanisms underlying the observed modifications were also investigated to elucidate their impact on target recognition. Different formulations of mAbs and ADCs, at clinically relevant concentrations and in saline or glucose solutions, were exposed to indoor light to simulate hospital conditions.
While mAbs preserved their overall conformational integrity, they exhibited increased aggregation and reduced target-binding capability. In contrast, ADC solutions showed visible colour changes and spectroscopic evidence of payload alteration, without detectable protein aggregation. Notably, although the cytotoxic payload and linker appeared to hinder aggregation, the presence of an additional photosensitive moiety represents an increased risk of instability.
Overall, these findings highlight the critical role of diluent composition, light exposure, and handling procedures in preserving the stability and therapeutic efficacy of mAbs and ADCs, while also revealing drug-specific differences in light-induced behaviour.

Acknowledgements: This research was supported by: IMI project, Joint Undertaking (JU) under grant agreement N° 101007939 (RealHOPE), and IOV - Veneto Institute for Oncology IRCCS.

Lorenzo Ferroni

Distinctive morpho-functional adaptations for photosynthesis in deep shade in the ancient vascular plant genus *Selaginella* (Lycopodiophyta)

L. Ferroni

Department of. Environmental and Prevention Sciences, University of Ferrara, Italy

Most current vascular plant species are euphyllophytes, with angiosperms representing the most diversified group. The remaining 1% of species belong to their sister clade, the lycophytes, from which they diverged ca. 415 Myr ago. Up to the Carboniferous period, forests of lycophytes dominated the Earth; subsequently, drop in air CO_2 concentration and temperature caused their extinction, except for a few species that survived up to present [1]. Among them, *Selaginella* is a very diverse genus, which thrives especially in the lower layers of equatorial rainforests. Under the selection pressure of humid, shaded environments, a major part of *Selaginella* species evolved among the most outstanding adaptations to living under light-limited conditions. In *Selaginella*, adaptive traits to the shade can be observed at all levels of organization, from leaf anatomy to cell morphology, from chloroplast structure to molecular and supramolecular organization of thylakoid complexes [2]. All these adaptations allow photosynthesis under low or very low irradiance characterized by a relative enrichment in the far-red component of the spectrum compared to red. In shade-adapted *Selaginella*, enhancement of light harvesting is achieved by a unique morphology of the epidermal cells, driving light to the single giant chloroplast that each of them hosts at the bottom. In the thylakoid membrane, the very abundant antenna system LHCII is associated with both photosystem II and I (PSII, PSI) and ensures high efficiency of light harvesting, as well as participates in photoprotection [3,4]. Shade plants are usually prone to photodamage when they are exposed to intense light, as can occur because of sun flecks filtering through the canopy. Nevertheless, a *Selaginella* species like *S. martensii* shows a much higher photoprotection capacity than one could expect for a sciaphilic plant. Excellent control of photosynthetic electron poise allows the preservation of PSI especially under intense or fluctuating light [5].

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Stefano Santabarbara

Evidence of bidirectional electron transfer in far-red light adapted Photosystem I.

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While it is established that in far-red light (FR)-adapted Photosystem II (PSII) at least one Chlorophyll (Chl)-*a* is replaced by Chl-*d*/*f* at the $ChlD_1$ position within the reaction centre (RC), the role of Chl-*f* in the FR-PSI RC remains controversial. Recent structural studies suggest that a single Chl-f replaces Chl-*a* at the $eC2_B$ (A_{-1B}) position on the B branch [1]. This substitution could introduce an energetic asymmetry favouring unidirectional electron transfer (ET), contrary to the widely accepted bidirectional mechanism of canonical Chl-a PSI RCs.
The ET directionality in FR-adapted *Chroococcidiopsis thermalis* PCC7203 PSI was investigated using light-induced ESE and TR-EPR spectroscopies at 80K and compared to white light (WL) grown controls. In FR-PSI at ambient redox conditions, the relaxation of the ESE stemming from the $[P_{700}^{+}A_{1}^{-}]$ radical pair (RP) shows bi-exponential decay with lifetimes of ~ 2.5 and ~ 25 µs and comparable amplitudes. In contrast, WL-PSI decay is dominated (>80%) by a ~35 µs component. ESEEM analysis for WL-PSI showed a single modulation frequency (dipolar interaction D = –168.6 µT, RP-partners distance R = 25.44±0.03 Å, $[P_{700}^{+}A_{1A}^{-}]$). FR-PSI requires an additional component (D = –196.1 µT, R = 24.19±0.02 Å, $[P_{700}^{+}A_{1B}^{-}]$). After illumination under reducing conditions at 220K, this component becomes dominant and the ESE decay mono-exponential (~ 3 µs) both in WL- and FR-PSI. Further, the Q-band TR-EPR spectrum of FR-PSI under non-reducing conditions differs from that of WL-PSI in the high field region. The FR-PSI spectrum can be reconstructed by a weighted sum of the WL-PSI spectrum and the one obtained after pre-illumination under reducing conditions. Taken together and recalling previous characterization in WL PSI [2, 3], these observations demonstrate the population of two RPs and provide strong support for bidirectional ET in FR-PSI that, in turn, bears consequences concerning the structural and functional organisation of the RC.

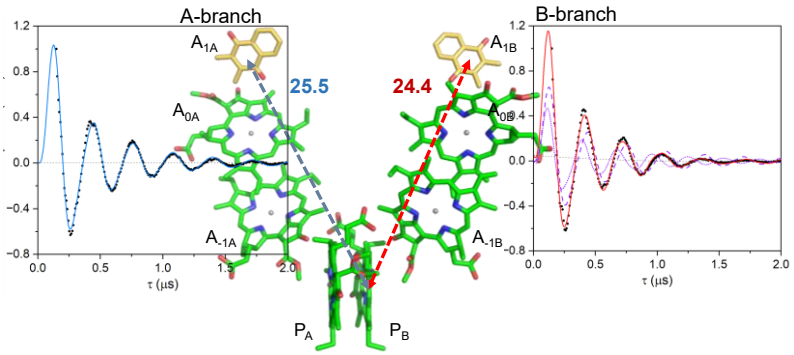


Fig 1. Experimental ESEEM traces and their fit showing the modulations corresponding to the $[P_{700}^{+}A_{1A}^{-}]$ and the $[P_{700}^{+}A_{1B}^{-}]$ radical pairs, together with the dipolar based estimation of distances within the structural model framework.

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Francesco Milano

In-field tomato growth under blue-depleted sunlight from a semi-transparent perovskite panel.

A. Paradiso[1], F. Milano[1], A. De Paolis[1], C. Ottaviani[2], P. Prete[3], P. De Padova[2,4], S. Caretto[1]

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Semi-transparent photovoltaic panels based on $Cs_2AgBiBr_6$ perovskite offer a strategy for concurrent energy production and crop cultivation, but the spectral reshaping of transmitted light raises fundamental questions about plant photoreceptor responses. We characterised the spectral irradiance transmitted by a yellow lead-free perovskite panel [1] and evaluated its effects on Micro-Tom tomato plants grown outdoors in southern Italy under two treatments: a glass control (C) and the yellow perovskite panel (Y). The Y panel substantially reduced PPFD relative to C, yet both values exceeded the optimal irradiance for this cultivar. The transmitted spectrum showed a steep absorption edge in the violet-blue region, with a marked reduction in blue photon flux: the B:R and B:G ratios fell significantly, while the R:FR ratio declined only marginally, remaining well within the full-sun range. This configuration – substantial cryptochrome-active blue reduction co-occurring with an essentially unaltered phytochrome signal – constitutes a condition of photoreceptor signal decoupling [2] with no natural equivalent under vegetated shade. Y plants responded with increased stem elongation, greater leaf number, and enhanced reproductive output, while total yield per plant was maintained. Fruit metabolite profiling revealed a selective increase in soluble sugars and a significant reduction in lycopene in Y fruits, while β-carotene remained unchanged, suggesting altered carbon partitioning rather than general suppression of secondary metabolism. Principal component analysis confirmed a consistent metabolic axis opposing sugar accumulation and lycopene content, with Y fruits clustering more tightly than C fruits in multivariate space.

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Maya D. Lambreva

Tiny diamonds, stronger cells: Hydroxylated nanodiamonds mitigate oxidative stress in *Chlamydomonas reinhardtii*

TK. Antal[1], AA Volgusheva[2], AA. Baizhumanov[2], GP. Kukarskikh[2], A. Mezzi[3], D. Caschera[3], G. Ciasca[4], MD. Lambreva[5]

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Widely used in biomedical and bioanalytical applications, detonation nanodiamonds (NDs) are emerging as versatile nanomaterials due to their small size, chemical stability, and highly tuneable surface chemistry [1]. Their surfaces can be readily functionalised, enabling control over properties such as dispersion, biocompatibility, and redox activity. Despite extensive study in animal and human cells, the effects of nanodiamonds on photosynthetic organisms remain largely unexplored, motivating this work. We explored the effects of hydroxylated nanodiamonds on the model green microalga *Chlamydomonas reinhardtii*, focusing on their phytotoxicity and antioxidant potential. NDs demonstrated low phytotoxicity across a broad concentration range and exhibited pronounced antioxidant behaviour. Their surface chemistry, dominated by hydroxyl functional groups, enables effective scavenging of reactive oxygen species, reducing cellular oxidative stress. Under stress conditions induced by chemical oxidants and high light, NDs preserve photosynthetic performance and support the repair of damaged photosynthetic components. This protective effect was most evident when cells were pre-exposed to nanoparticles, suggesting close interaction with cellular structures and possible internalisation [2].

Overall, hydroxylated nanodiamonds may act as efficient, tuneable antioxidants in photosynthetic cells. Their unique combination of stability, surface reactivity, and low toxicity highlights their potential as functional nanomaterials for improving cellular resilience. These findings open new perspectives for the application of engineered NDs in algal biotechnology and sustainable photosynthetic systems, while emphasising the importance of surface functionalisation in defining their biological effects.

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Rossella Labarile

Chromatophore-based biohybrid architectures for solar-pumped laser systems: role of scattering in optical characterization

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Chromatophores, isolated from the photosynthetic purple bacterium *Rhodobacter sphaeroides,* are employed as functional components in biohybrid systems for solar-pumped lasers, based on photosynthetic antenna complexes [1, 2]. These assemblies exploit the exceptional light-harvesting efficiency and ultrafast energy transfer dynamics of bacterial photosynthesis, with the aim of contributing to optical amplification when chromatophores are integrated into supramolecular architectures incorporating suitable lasing elements.
In this context, accurate spectroscopic characterization is essential for understanding their optical properties and energy-transfer behavior. However, light scattering arising from the vesicular and heterogeneous nature of chromatophore suspensions represents a critical challenge, as it can significantly distort absorption spectra and compromise the quantitative interpretation of optical data [3, 4].
To address this issue, scattering contributions were systematically investigated using two complementary approaches. First, single-wavelength scattering measurements were performed using an 800 nm laser source to quantify elastic scattering independently of pigment absorption. Second, a full-spectrum correction procedure was applied to account for wavelength-dependent scattering effects across the entire spectral range.
The combined implementation of these methodologies enabled a robust assessment and effective mitigation of scattering artifacts, significantly improving the reliability, accuracy, and comparability of spectroscopic analyses. This integrated strategy provides a solid basis for the quantitative characterization of chromatophore-based systems and supports the development of bio-inspired photonic media capable of converting solar energy into coherent light emission.

Project APACE - Towards a bio-mimetic sunlight pumped laser based on photosynthetic antenna complexes (Project n. 101161312) funded by Horizon-European Innovation Council is acknowledged.

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Valentina Rapozzi

Nitric oxide, Nrf2 signaling and tumor hypoxia: Interconnected determinants of resistance and response in photodynamic therapy

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Photodynamic therapy (PDT) is a clinically established anticancer treatment based on light-activated photosensitizers that generate reactive oxygen species (ROS), leading to oxidative tumor damage. Despite its efficacy, PDT is often limited by adaptive stress responses that promote tumor survival and resistance. Key regulators of this adaptive response include nitric oxide (NO), Nrf2-dependent antioxidant signaling, and tumor hypoxia, which form an interconnected network influencing therapeutic outcome.

NO plays a dual, concentration-dependent role in PDT. At low levels, it promotes cytoprotection by modulating mitochondrial function, redox homeostasis, and pro-survival signaling pathways, thereby contributing to treatment resistance and tumor aggressiveness. In contrast, high NO levels can enhance oxidative and nitrosative stress, potentiating PDT-induced cytotoxicity [1].

A central adaptive mechanism involves activation of the Nrf2 pathway, a master regulator of antioxidant and detoxification responses. Nrf2-driven gene expression enhances cellular defense against oxidative stress, reduces ROS-mediated damage, and supports tumor cell survival following PDT exposure, contributing to therapy resistance [2].

Tumor hypoxia further limits PDT efficacy by reducing oxygen availability required for ROS generation. In addition, hypoxia activates adaptive programs such as angiogenesis, metabolic reprogramming, and resistance to oxidative stress. Emerging evidence highlights extensive crosstalk between hypoxia signaling, NO production, and Nrf2 activation, collectively shaping tumor adaptation to PDT [3].

Overall, the interplay between NO signaling, Nrf2-mediated antioxidant defense, and tumor hypoxia critically determines PDT response. Targeting these interconnected pathways may provide novel combinatorial strategies to modulate redox balance, overcome adaptive resistance, and improve the therapeutic efficacy of PDT in cancer.

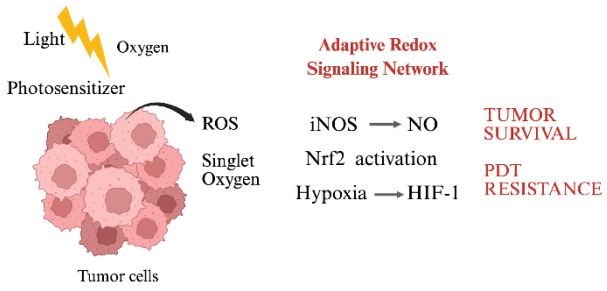


Fig 1. Adaptive redox and hypoxic signaling pathways underlying resistance to photodynamic therapy.

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Thenesia Govender

Development of Multimodal, light-activated NO-based conjugates for triple-negative breast cancer treatment

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Triple-negative breast cancer (TNBC) is the most aggressive type of breast cancer. It is characterized by poor prognosis, high metastatic potential, and a lack of targetable receptors which limits the development of targeted therapeutics, leaving chemotherapy as the primary treatment [1]. Androgen receptor (AR) is widely expressed in breast cancer, particularly in the LAR subtype of TNBC, providing a key opportunity for the development of targeted therapeutic strategies [2, 3].

Photodynamic therapy (PDT) is a promising cancer treatment due to its intrinsic selectivity. Nitric oxide (NO) therapy is an attractive yet complex approach, reflecting its dual role in cancer biology: NO promotes tumour growth at low concentrations but exerts anticancer effects at higher levels [4]. Therefore, precise control of NO release is essential. Importantly, NO activity is oxygen-independent, enabling efficacy in the hypoxic tumour microenvironment (TME). Combination strategies are increasingly explored to enhance therapeutic outcomes: integrating NO donors with PDT enables synergistic effects via ROS generation and controlled NO release. Additionally, conjugation with chemotherapeutic agents may further improve selectivity, modulate drug activity, and enhance cancer cell sensitivity to treatment.

This work investigates combining NO-based therapy with PDT or chemotherapy, focusing on multimodal conjugates for TNBC. Antiandrogen NO-donor moieties were linked to paclitaxel (PTX) or pheophorbide *a* (Pba) using biocompatible, cleavable linkers, enabling controlled activity and targeted therapeutic effects (Figure 1). Our results demonstrate that NO-donor–Pba conjugates can efficiently generate both NO and reactive oxygen species, with the relative contribution depending on the irradiation conditions (white *vs* red light), thus enabling tuneable multimodal activity. In addition, kinetic studies performed on NO-donor–PTX conjugates under TME mimicking conditions revealed a sustained and controlled PTX release over time. Preliminary biological data show that, upon white-light irradiation, NO-donor–Pba conjugates induce a significantly greater reduction in cell viability in different TNBC cell lines compared to Pba alone, confirming an enhanced phototherapeutic effect.

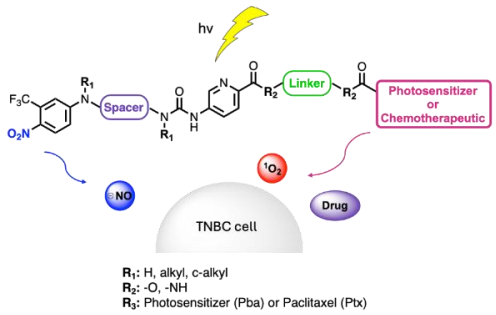


Fig 1. Schematic representation of molecular conjugates bearing an antiandrogen NO-releasing moiety connected with either a photosensitizer or a chemotherapeutic drug through a bio-cleavable linker.

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Erna Tintor

CAIX-Targeted inhibitor-photosensitizer conjugates for enhanced photodynamic efficacy under hypoxic tumor conditions in triple-negative breast cancer cells

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Photodynamic therapy (PDT) is limited by tumor hypoxia, which reduces oxygen-dependent ROS generation and significantly impairs therapeutic efficacy in aggressive tumors such as triple-negative breast cancer (TNBC) [1,2]. To address this limitation, we developed a benzophenothiazinium (EtNBS) photosensitizer operating via a Type I mechanism, enabling oxygen-independent radical formation and sustained ROS production under hypoxic conditions [3]. To enhance tumor selectivity, the system was functionalized with benzenesulfonamide, a carbonic anhydrase IX (CAIX)-targeting moiety, with the aim of exploiting the strong overexpression of CAIX in hypoxic and acidic tumor microenvironments [4,5].

The photosensitizer was evaluated in two different CAIX expression level cellular lines, MCF-7 (low level) and MDA-MB-231 (high level, TNBC) cells. The CAIX-targeted construct (DAB460) exhibited significantly higher photocytotoxicity in MDA-MB-231 cells compared to MCF-7, confirming CAIX-dependent selective uptake.

Functional validation using acetazolamide (AAZ), a CAIX inhibitor, demonstrated a context-dependent modulation of PDT response. In CAIX-overexpressing MDA-MB-231 cells, AAZ enhanced the photodynamic effect of DAB460, suggesting synergism between CAIX inhibition, pH dysregulation, and ROS-mediated cytotoxicity.

These findings align with recent advances highlighting CAIX as a validated target for hypoxia-adapted PDT strategies [5,6].

Overall, this study demonstrates that combining Type I photosensitizer with CAIX-targeting strategies overcomes hypoxia-induced resistance, providing a robust platform for selective PDT in aggressive tumors such as TNBC.

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Cosmin Butnarasu

Lighting up mucins: development of polymethine dyes for mucin-responsive sensing in pancreatic cancer

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Aberrant mucin expression is a characteristic feature of several epithelial malignancies, including pancreatic ductal adenocarcinoma, where mucin-associated glycoproteins are being explored as biomarkers for diagnosis, prognosis and therapy. However, mucin detection in biological fluids remains analytically challenging because of mucin heterogeneity, extensive glycosylation, high molecular weight and interference from abundant serum proteins.

Here, we investigated polymethine dyes as mucin-responsive optical probes, focusing on squaraine and cyanine scaffolds with different substituents, lipophilicity and aggregation behavior [1-3]. A panel of dyes was characterized by UV–Vis absorption and fluorescence spectroscopy in aqueous media, using commercial mucins as a model mucin. Selectivity was evaluated against albumin and additional serum- or tissue-associated proteins, while selected candidates were tested in serum-derived matrices to assess analytical feasibility.

The dyes displayed strongly structure-dependent photophysical behavior, with aggregation-associated quenching in aqueous medium and mucin-induced spectral changes. The squaraine series provided useful structure–property information, suggesting that lipophilicity and aggregation behavior are key parameters controlling fluorescence turn-on, while the cyanine series revealed a complementary color-shift response upon mucin interaction.

Although direct detection of mucins at serum-relevant levels remains challenging because of low biomarker abundance and matrix interference, these findings provide a rational basis for the future design of more selective and sensitive mucin-responsive dyes and support further development of fluorescence/colorimetric platforms for pancreatic cancer biomarker-oriented research.

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Federica Randisi

BODIPY-loaded liposomes enhance cellular uptake and PDT efficacy in 2D and 3D models.

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Photodynamic therapy (PDT) is a cancer treatment that combines a photosensitizer (PS), light of an appropriate wavelength, and molecular oxygen to generate reactive oxygen species (ROS) responsible for malignant cell death. PDT efficacy is strongly influenced by PS accumulation in tumors, driving the development of third-generation PSs, including novel PSs with targeting strategies and nanotechnology-based delivery systems [1]. Among these, BODIPYs (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene) have gained attention due to their high extinction coefficients, environmental stability, resistance to photobleaching, and higher light-to-dark toxicity ratios [2]. Within available nanocarriers, liposomes are particularly attractive due to their low toxicity, biodegradability, and high biocompatibility arising from their lipid composition. Liposomes have demonstrated the ability to enhance drug permeability across biological membranes and to provide sustained-release profiles [3].

In the present study, two BODIPY derivatives differing in the position of a methyl ester group on the meso-phenyl ring were designed and synthesized to evaluate structure-activity relationships. Both compounds were incorporated into liposomes, and their enhanced uptake into colorectal and ovarian cancer cell lines, compared to free compounds, was confirmed. The effects of liposomal formulations were then evaluated in 2D and 3D cellular models, assessing cell viability, ROS production, induction of necrotic, apoptotic, and ferroptotic cell death, and inhibition of cell migration. The liposomal formulations induced cancer cell death through both canonical and non-canonical mechanisms, retained strong activity also in 3D tumor models, and effectively impaired migratory capacity.

These findings highlight the potential of liposome-encapsulated BODIPYs as effective PDT agents, to enhance cellular uptake and exert significant antitumor activity through multiple cell death pathways. Moreover, the methyl ester group at the meso phenyl ring represents a versatile synthetic handle for future functionalization with targeting moieties, such as antibodies or peptides, potentially enabling the development of third-generation, tumor-targeted PS derivatives and warranting further preclinical investigation.

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Francesca Bianco

Orai1 inhibition and PDT: novel combination therapy for Pancreatic Ductal Adenocarcinoma

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Resistance to conventional chemotherapies drastically reduces pancreatic ductal adenocarcinoma (PDAC) 5-years survival rate[1]. This depends on tumor microenvironment (TME) characteristics, particularly its stiffness, that impairs vascularization and nutrients diffusion, leading to metabolic reprogramming and TME acidification. Overall, extracellular pH(pH_e) lowering promotes the onset of more aggressive and chemotherapy resistant cells, as well as Ca^{2+} signaling alterations[2-4]. Ca^{2+} channels, including Orai1, have been described as sensitive to acidic pH_e[5], even though their role in chemoresistance is still poorly understood. Recently, alternative therapies are under investigations, including Photodynamic therapy (PDT), that exploits photosensitizers (PSs) molecules that induces light-dependent, tumor-specific cell death. We recently demonstrated tumors phototoxicity of red-absorbing PS Br-SQ-C4[6], therefore, in the present work we **aim** to characterize the role played by Orai1 in PDAC chemoresistance and the potential combination of Br-SQ-C4-dependent PDT and Orai1 inhibition as novel PDAC therapy.

Panc-1 and Mia PaCa-2 cell lines were kept in physiological pH_e(7.4, CT) and chronically exposed to acidic pH_e(6.6, pH_e-selected)[4]. The latter displayed higher Orai1-mediated Store Operated Ca^{2+} Entry(SOCE), Ca^{2+} oscillations frequency and chemoresistance compared to CT. Br-SQ-C4 is phototoxic in both Panc-1 and Mia PaCa-2 cell, localizes into endoplasmic reticulum and triggers Ca^{2+} and ROS signals, which interplay differs in CT and pH_e-selected cells. Moreover, Orai1 played a crucial role in Br-SQ-C4 phototoxicity, indeed its pharmacological inhibition enhanced the PS phototoxicity.

Overall, these findings demonstrate Orai1 involvement in PDAC chemoresistance. Thus, Orai1 inhibition, by enhancing Br-SQ-C4 phototoxicity, paves the way for novel combination therapies involving PDT and Ca^{2+} channels modulation.

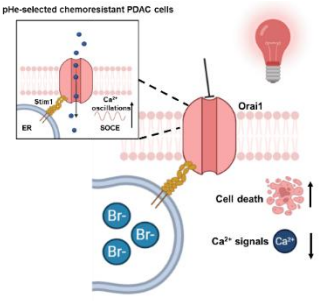


Fig 1. Graphical Abstract (created with BioRender).

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Sara Cascone

Development of anionized albumin formulations for macrophage-selective photoimmunotherapy

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The tumor microenvironment (TME), characterized by chronic inflammation and a complex interplay of host cellular components, plays a pivotal role in cancer development and progression. Among TME constituents, macrophages exhibit remarkable plasticity, polarizing toward distinct functional phenotypes depending on local stimuli. While pro-inflammatory M1-like macrophages exert anti-tumoral activities, tumor-associated macrophages (TAMs) predominantly acquire an M2-like, immunosuppressive phenotype that actively supports tumor growth [1]. Reprogramming or selectively depleting M2-like TAMs therefore represents a promising therapeutic strategy.

To this end, we developed a macrophage-selective drug delivery platform based on anionized bovine serum albumin (BSA), exploiting the preferential uptake of small, negatively charged particles by macrophages [2]. Increased surface negativity was achieved by reacting BSA with succinic or maleic anhydride under optimized conditions, yielding both single-protein and nanoparticle formulations. Cellular internalization was first assessed by flow cytometry using CF488 as a fluorescent probe. Anionized nanoparticles displayed markedly superior uptake compared to single protein formulation and their non-anionized counterparts. In co-culture experiments, macrophages internalized the constructs significantly more efficiently than colorectal cancer cells, confirming cellular selectivity. The most promising formulation, namely succinylated BSA nanoparticles, was loaded with the photosensitizer temoporfin [3] and evaluated for macrophage photoablation. Cell viability assays revealed a significant concentration-dependent cytotoxic effect upon irradiation, whereas non-irradiated controls remained unaffected. The succinylated formulation showed an EC_{50} of 400 nM. Overall, these findings provide a proof-of-concept for anionized albumin nanoparticles as a biocompatible, macrophage-targeted platform for photoimmunotherapy. Future studies will focus on photo-mediated macrophage repolarization strategies, and on expanding the payload repertoire to poorly bioavailable compounds active in photodynamic ablation or phenotypic modulation of immunosuppressive TAMs.

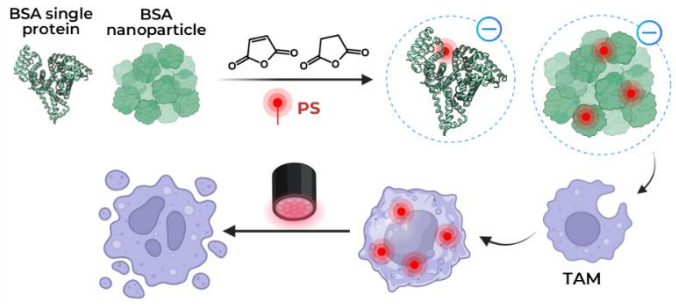


Fig 1. Synthesis and PDT mechanism of action of macrophage-selective anionized BSA formulations

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Melisa Ciglarić

Synthesis of cationic AB_3 *meso*-(4-(*N*,*N*-diethylamino)phenyl)porphyrins for *in vitro* studies on melanoma cells

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Photodynamic therapy (PDT) is a promising therapeutic approach based on the activation of photosensitizers by light of an appropriate wavelength, resulting in the generation of reactive oxygen species that induce selective damage to target cells. Owing to the need for more efficient photosensitizers, particular interest has been directed toward amphiphilic porphyrin systems with improved cellular uptake [1].

Previous studies have shown that increasing the lipophilicity of porphyrins through the introduction of long alkyl chains can significantly influence cellular uptake and photodynamic efficiency [2]. This has been demonstrated in our previous study with *N*-methylated tricationic pyridiniumporphyrins with different hydrophilic–lipophilic balance profiles in PDT studies on melanoma cell lines. In particular, porphyrins with an alkyl chain with 14 C atoms exhibited pronounced selectivity toward tumor cell lines, whereas the analogue with 18 C atoms showed the highest overall cytotoxicity across all tested cell lines [2].

In this work, our aim was to synthesize analog amphiphilic porphyrins, but incorporating *N*,*N*-diethylaniline substituents instead of pyrid-3-yl groups suitable for quaternization of nitrogen atoms. First step was the Adler Longo condensation to obtain AB_3 porphyrins with three *N*,*N*-diethylaniline and one 4-acetamidophenyl substituents, followed by hydrolysis of acetamido to amine group. Long alkyl chains (with 14 and 18 C atoms) were conjugated via nucleophilic acyl substitution reaction using acyl chlorides ($C_{13}H_{27}COCl$ and $C_{17}H_{35}COCl$), and *N*-methylation was performed with methyl iodide to yield the corresponding quaternized amphiphilic porphyrin derivative.

During the study, it was observed that the porphyrins synthesized before methylation exhibit the formation of hyperporphyrin species under acidic conditions, accompanied by a bathochromic shift toward the red region of the electromagnetic spectrum [3]. These properties may be particularly relevant for PDT due to more efficient excitation at longer wavelengths that are known for improved tissue light penetration. Alongside the synthesis and spectroscopic characterization (UV-Vis and fluorescence spectroscopy) of all new compounds, preliminary MTT screening results on melanoma cell line and non-tumor cell line will also be presented.

Acknowlegments: This work was supported by the Croatian Science Foundation under the project number HRZZ-IP-2022-10-7000.

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Giulia Giugliano

Machine learning-driven discovery of novel photosensitizers for photodynamic therapy

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Photodynamic therapy is a minimally invasive cancer treatment associated with fewer side effects than chemotherapy and radiotherapy.[1] Its broader clinical use is limited by the scarcity of efficient photosensitizers. *De novo* development is hindered by time-consuming synthesis, heavy chemical use, and the high computational cost of predicting excited-state properties that govern therapeutic activity. We present a machine learning-driven pipeline to rapidly identify new photosensitizers from drug-like chemical libraries. Using X-MACE,[2] a message-passing neural network trained to predict key photophysical properties, we screen thousands of molecules from therapeutically relevant databases in minutes, a task that would take decades with conventional quantum-chemical excited-state methods. Experimental validation of pyrvinium, X-MACE top-ranked compound, demonstrates strong light-enhanced cytotoxicity across four cancer cell lines (CAL-27, A-431, HT-29, and MDA-MB-231), with IC_{50} improvements ranging from 24 to 302-fold upon photoactivation.[3] Overall, this integrated framework shows how machine learning can accelerate and streamline photosensitizer discovery, identifying therapeutically active compounds and supporting the development of more effective photodynamic therapy agents.

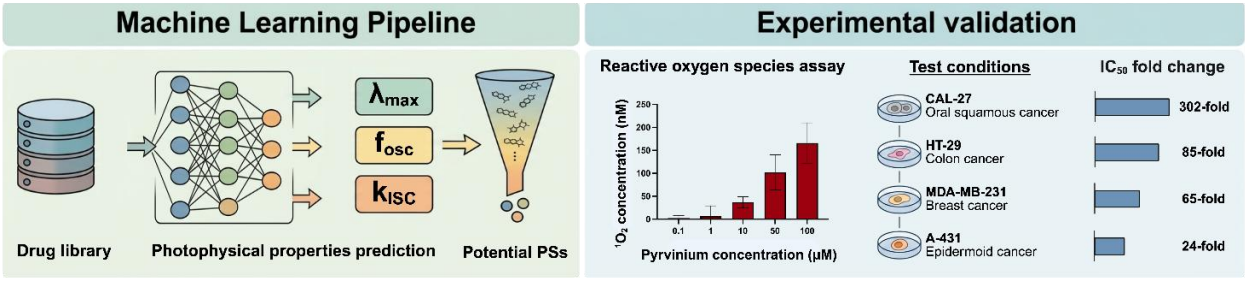


Fig 1. Workflow of the integrated computational-experimental platform.

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Martina Mušković Lukić

Impact of melanin pigment and hypoxic conditions on (photo)cytotoxicity of amphiphilic *N*-methylated tripyridiniumporphyrins with alkyl chains of different length on melanoma cell lines

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Melanoma is the leading cause of death among skin cancers, largely due to diagnosis at intermediate or advanced stages of the disease. In photodynamic therapy (PDT), melanoma exhibits increased resistance, primarily due to the presence of pigment melanin, which absorbs light in the visible part of the EM spectrum and possesses antioxidant properties. Other melanoma resistance mechanisms include ATP-binding cassette (ABC) transporter-mediated drug efflux and dysregulation of apoptotic pathways [1]. Moreover, hypoxia is a common feature of solid tumors, including melanoma, where it contributes to tumor heterogeneity, promotes metastatic progression and alters metabolic processes [2]. Therefore, PDT in melanoma represents a therapeutic challenge that must act on two fronts: overcoming melanin-associated resistance and addressing hypoxic conditions.

Our previous work on amphiphilic *N*-methylated porphyrins showed significant cytotoxicity, with IC_{50} <1 μM for porphyrins conjugated with alkyl chains longer than 14 C atoms after 30-min irradiation with red light (λ = 643 nm, fluence 2 mW/cm^2). Furthermore, porphyrin with 14 C atoms showed highr selectivity towards both melanoma cell lines tested, A375 and MeWo [3].

In this work, we present a series of porphyrins with alkyl chains 13, 14, 15, 16 and 17 C atoms long, which includes two new compounds. Their characterization and *in vitro* activity evaluation on the non-pigmented (A375) and on the highly-pigmented melanoma cell line (B16F10) will be presented. For the B16F10 cell line experiments were conducted under both melanizing (DMEM) and non-melanizing (Ham's F10) cell culture conditions to indicate the difference in melanin production, and the human foreskin fibroblasts (HFF) served as the non-tumour control cell line. Phototoxicity results under both normoxic condition and hypoxic condition achieved using hypoxia chamber will be discussed.

Funding: This work was supported by the Croatian Science Foundation through the project HRZZ-IP-2022-10-7000.

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Piergiacomo Calzavara Pinton

A lifetime in science: reflections on light based therapies and dermatological research

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UVB (both narrowband, NB, and broadband, BB) phototherapies and PUVA (Psoralen plus UVA) photochemotherapy have seen great momentum in Dermatology in the decades from 1970 to 2010. They were considered first line therapies for many common skin disorders like psoriasis, prurigo nodularis and atopic dermatitis. However, from the end of the last century, a growing number of biologicals became available for these indications. Their efficacy is very high, and tolerability and safety are very good. Therefore, they are suitable for the long-term management of these skin disorders as well as for the prevention of their systemic complications. In addition, they are patient-friendly because subcutaneous injections are needed at intervals ranging from 2 weeks to 3 months, they are not as time consuming as phototherpy is and, in Italy, they are cheaper (for the patients) than phototherapy because of the "ticket". Their cost (for the NHS) was very expensive at the beginning but, at present, biosimilars are equally effective and very cheap. As a matter of fact, the number of Dermatology Departments equipped with a phototherapy center, declined progressively and now it is present only in few big hospitals. However, phototherapy remains the first choice treatment for several skin disorders like patch-stage mycosis fungoides, polymorphic light eruption, morphea, liche planus and others. The main challenge now is to identify the profile of patients for which phototherapy has mantained a therapeutic value.
In a broader sense, also photodynamic therapy (PDT) is a form of phototherapy. PDT with ALA or MAL remains one of the best treatments for patients with multiple actinic keratoses, but new indications have not been approved so far, and the investigation of new photosensitive molecules is discouraged by the very high costs of medical research now.

Isacco Cattaneo

Real-life experience from a tertiary phototherapy center on solar urticaria: clinical features, management, and long-term outcomes from a twenty-year cohort

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Solar urticaria (SU) is a rare chronic photodermatosis characterized by the rapid onset of pruritic wheals after exposure to ultraviolet (UV) or visible light, often severely impairing quality of life and daily activities.[1;2] Antihistamines frequently provide only partial relief, whereas tolerance-induction phototherapy (photohardening) is considered the main therapeutic approach in persistent disease, although long-term real-world evidence remains limited.[3-7] This study evaluated the clinical features and long-term outcomes of desensitizing phototherapy in patients with confirmed SU treated in a tertiary referral center over a twenty-year period.

This retrospective observational study included patients evaluated for suspected SU between 2005 and 2025. Among 167 assessed individuals, 53 met inclusion criteria, including positive phototesting for UVA and/or UVB reactivity, completion of at least one phototherapy cycle, and adequate follow-up. Baseline assessment included clinical history, laboratory tests, and phototesting with determination of minimal urticarial dose (MUD) and/or minimal erythemal dose (MED). Phototherapy protocols were individualized according to the provoking spectrum.[7] Patients with UVA sensitivity generally received NB-UVB phototherapy, whereas UVB-reactive patients underwent UVA phototherapy following cross-spectrum photohardening principles.

The cohort included 30 males and 23 females with a mean age of 45±13 years. The provoking spectrum was UVA in 47%, UVB in 43%, and mixed in 10% of patients, while visible-light testing was positive in 23%. Complete remission was achieved in 62% of patients, partial improvement in 28%, and no response in 9%, resulting in an overall clinical benefit in 91% of cases. Phototherapy was well tolerated, with only mild transient adverse events reported. Median follow-up was 4.7 years, and remission persisted in 58% of patients, while relapses occurred after a mean of 4.2 years. Long-term remission was associated with a marked increase in phototolerance. Overall, desensitizing phototherapy with UVA or NB-UVB proved to be an effective, safe, and durable first-line treatment for confirmed solar urticaria.

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Mariateresa Rossi

Photoprotection in inflammary dermatoses

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Photoprotection is a key component in the management of inflammatory dermatoses, particularly in conditions where ultraviolet and visible radiation can trigger, worsen, or prolong cutaneous inflammation. Diseases such as lupus erythematosus, rosacea, atopic dermatitis, psoriasis, dermatomyositis, and polymorphic light eruption may show variable degrees of photosensitivity, making light protection an essential preventive and therapeutic strategy. Ultraviolet A and B radiation promote oxidative stress, immune dysregulation, barrier impairment, and cytokine release, contributing to disease flares and post-inflammatory hyperpigmentation.[1]

Increasing evidence also highlights the role of visible light, especially high-energy visible light, in inducing oxidative stress, erythema, pigmentation, and inflammatory responses, particularly in patients with darker phototypes or pigmentary-prone inflammatory dermatoses. For this reason, broad-spectrum photoprotection should include not only UVA and UVB coverage, but also protection against visible light when clinically relevant.[2]

Effective photoprotection requires a comprehensive approach combining behavioral measures, protective clothing, and regular use of broad-spectrum sunscreens. Tinted sunscreens containing iron oxides are particularly useful because they improve protection against visible light and may reduce post-inflammatory hyperpigmentation. Modern formulations should provide high protection, good tolerability, and cosmetic acceptability to improve adherence, especially in patients with sensitive or inflamed skin.[3]

Photoprotection should therefore be considered an integral part of personalized dermatological care. Tailoring sunscreen choice to the specific inflammatory disorder and individual phototype can reduce exacerbations, improve treatment outcomes, and enhance quality of life.

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Luigi Spiazzi

Physics in photodermatology: quantitative imaging and AI

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Clinical photodermatology is undergoing a profound evolution driven by the integration of advanced optical technologies, quantitative imaging, artificial intelligence and the progressive digitalization of clinical workflows. In this context, light is no longer only a therapeutic or diagnostic tool, but increasingly represents a complex source of biological, morphological and functional information integrated into modern clinical decision-making. In everyday hospital practice, the use of dermatologic imaging systems, laser technologies, phototherapy devices, multispectral acquisitions and digital platforms for longitudinal lesion assessment is progressively transforming the way skin diseases are observed, measured and monitored. At the same time, artificial intelligence is opening new perspectives in image analysis, risk stratification and support for diagnostic and therapeutic processes.

This transformation also introduces important challenges related to acquisition standardization, image quality and reproducibility, data integration, clinical validation of digital tools and the management of increasing technological complexity. Within this evolving scenario, quantitative approaches, light–tissue interaction and multidisciplinary integration are becoming increasingly relevant for translating advanced photobiological technologies into routine clinical practice..

We will provide a hospital-based perspective on the relationship between physics, optical technologies and dermatologic clinical practice, with particular attention to the emerging role of quantitative imaging and artificial intelligence in contemporary photodermatology.

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Alessandro Franzini

Light and edema: An Unexpected association

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Background

Isolated solar angioedema is a rare photodermatosis characterised by recurrent angioedema triggered by sun exposure without urticarial wheals (1). A previously published five-patient case series from our institution represented one of the major contributions to the current knowledge of this rare condition (1). Because of its rarity and atypical presentation, diagnosis may be difficult and therapeutic strategies are not well established (2).

Presentation

We report the case of a female patient presenting with recurrent episodes of edema involving the upper lip, eyelids, and acral sites, associated with deep stinging pain developing approximately 10 minutes after sun exposure, lasting up to 72 hours. The episodes occurred exclusively following solar exposure throughout the year. An extensive diagnostic workup excluded hereditary and acquired forms of angioedema, as well as other photosensitivity disorders. Phototesting findings supported the diagnosis of isolated solar angioedema.

Discussion

The absence of wheals, the prolonged duration of edema, and the rarity of the condition may complicate recognition of this entity. In our patient, the clear temporal relationship with sun exposure together with supportive phototesting findings provided the key diagnostic clues.

Conclusion

This case highlights an exceptionally rare form of photodermatosis presenting as isolated solar angioedema with mucosal and acral involvement. Greater awareness of this uncommon condition is essential to ensure prompt diagnosis and appropriate management. Oral prednisone, photohardening protocols, and omalizumab may represent promising therapeutic strategies.

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Venturini Marina

Photodynamic therapy with topical zinc phthalocyanine RLP068/Cl for moderate-to-severe papulopustular acne: A pilot study

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Acne vulgaris is a highly prevalent inflammatory disease of the pilosebaceous unit, often requiring prolonged and repeated therapeutic courses. Conventional treatments, including topical agents, systemic antibiotics, hormonal therapies, and isotretinoin, may be limited by tolerability, contraindications, adherence issues, and increasing concerns regarding antibiotic resistance. Zinc phthalocyanine derivatives, including RLP068/Cl, are promising second-generation photosensitizers because of their photodynamic activity and potential antibacterial efficacy. This pilot study evaluated the efficacy, safety, and tolerability of PDT with topical RLP068/Cl in patients with moderate-to-severe facial acne vulgaris.

We conducted a prospective monocentric pilot study including 10 patients with moderate-to-severe facial acne. Eligible patients underwent topical application of RLP068/Cl gel 0.3% after cleansing of the treatment area, followed by 30 minutes of occlusion. The treated areas were then illuminated with red LED light at 630 nm, delivering 60 J/cm² over 8 minutes. Treatment was performed twice weekly, with sessions spaced 3–4 days apart, and the total number of sessions was individualized according to clinical response. Acne severity was assessed using the Global Acne Grading System (GAGS) at baseline, end of treatment, and 3-month follow-up. RLP068/Cl-PDT induced a clinically meaningful reduction in acne severity, with mean GAGS score decreasing from 20.9 at baseline to 12.9 after treatment and 7.5 at 3-month follow-up. Treatment was very well tolerated, with low procedural pain (VAS 0.71 ± 0.48) and high patient satisfaction (mean Likert score 3.3/4). Adverse events were mild and transient, mainly short-lasting erythema. These preliminary findings suggest that RLP068/Cl-mediated PDT may represent a promising, well-tolerated therapeutic option for moderate-to-severe acne.

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Alessio Colleoni

Photoswitchable glycomimetics enable precision targeting of LecB in *Pseudomonas aeruginosa*

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Antimicrobial resistance (AMR) is a major global health challenge, particularly in hospital-acquired infections, where biofilm formation plays a central role in persistent and treatment-refractory bacterial communities. Biofilms establish a protective microenvironment that enhances microbial survival, limits antibiotic penetration, and facilitates horizontal gene transfer. Bacterial adhesion proteins are essential for biofilm initiation and maturation, mediating initial surface attachment and intercellular interactions, and thus represent attractive targets for alternative anti-infective strategies. This work focuses on LecB, an outer membrane lectin from *Pseudomonas aeruginosa* that contributes to virulence and biofilm stability through its high-affinity carbohydrate-binding properties. LecB mediates interactions with both bacterial surface glycoconjugates and extracellular polysaccharides, thereby supporting adhesion and structural integrity within the biofilm matrix [1-2].

We report the development of novel photoswitchable glycomimetic ligands designed to modulate LecB activity in a light-dependent manner. These compounds aim to enable reversible and spatiotemporally controlled regulation of bacterial adhesion processes. Starting from an initial photoswitchable *hit compound* that provided proof of concept for LecB targeting, a computationally guided *hit-expansion* strategy was employed to explore chemical space and optimize binding properties. This structure-based design approach led to the identification of several photoswitchable candidates with improved affinity, especially in the *cis*-enriched state relative to the reference compound [3].

Overall, this work highlights the potential of integrating light-responsive small molecules with computational design strategies to achieve reversible control over bacterial–host interactions with novel high-affinity modulatos, offering a promising framework for the development of innovative antibiofilm strategies to address AMR.

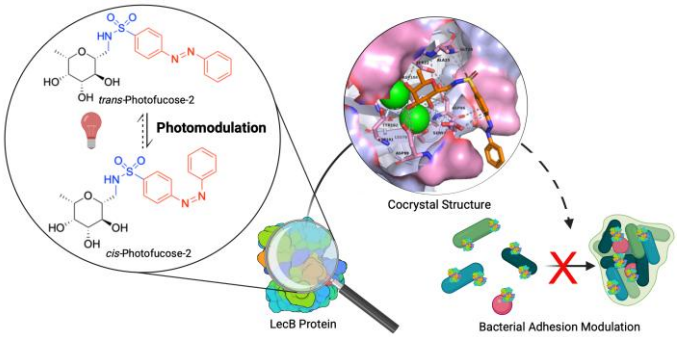


Fig 1. Photoswitch-*driven* LecB Protein Modulation.

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Mathias O. Senge

Molecular and formulation strategies for photosensitizer design

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A clinically useful photosensitizer must have the appropriate photophysical characteristics, allow for control of the relevant parameters via external stimuli, have a pharmacological profile appropriate for the target disease, and, ideally, elicit an immune response [1]. From a molecular design perspective, it would be ideal if some or all these criteria could be imprinted into a small molecule drug without having to resort to complex multimodality systems or multicomponent formulations. The presentation will give an overview about contemporary synthetic organic approaches in photosensitizer design focusing on the role of molecular shape and specific functional groups in improving PDT efficacy. Synthetic organic chemistry methods were used to prepare: a) BODIPY systems capable of excited state triplet formation via charge-separated states [2]; b) BODIPY and porphyrins capable of binding and releasing singlet oxygen [3]; c) atropisomerically pure photosensitizers and strapped porphyrins as mimics thereof with enhanced cellular uptake [4,5]; d) mTHPC (Temoporfin), BODIPY, and protoporphyrin derivatives with functional groups suitable for linking to hydrogels [6]. Photophysical measurements were performed to establish the ground and excited state properties of the novel photosensitizers, while in vitro cell biological (melanoma and colon carcinoma cells) and in vivo (mice) studies were used to investigate the PDT efficacy of the novel systems. Rational planning of the molecular structure and reactivity in a synthetic molecular engineering approach was used to establish novel photophysical activation pathways for photosensitizers and to enhance cellular uptake and tissue targeting in PDT. While it is still difficult to design an optimal photosensitizer, the various design criteria outlined herein are suitable to improve many properties of light-activated drugs.

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Nika Škokić

Impact of Zn(II) and Cu(II) chelation with methylated tetrakis pyridinium-3-yl porphyrin on antimicrobial properties and photodynamic inactivation

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In recent years, the rise in antimicrobial resistance (AMR) has increased the need for alternative therapeutic approaches to conventional antibiotic treatment. Water environments can serve as reservoirs of opportunistic pathogens, many of which are associated with hospital-acquired infections and are capable of forming biofilms. [1] Antimicrobial photodynamic therapy (aPDT) has gained attention due to its mechanism based on activation of, per se non-toxic photosensitizer (PS) by visible light which leads to formation of singlet oxygen ($^1O_2$) and reactive oxygen species (ROS) leading to oxydation of bacterial genetic material and cell apoptosis. [2] Cationic porphyrins have, so far, shown significant potential in the photodynamic inactivation (PDI) of opportunistic bacteria since their positive charge promotes stronger electrostatic interactions with Gram-negative bacteria. [3,4]

In this study, cationic 5,10,15,20-tetrakis(*N*-methylpyridinium-3-yl) porphyrin tetrachloride and its derivates coordinated with Zn(II) and Cu(II) ions were synthesized and their structures were confirmed by NMR spectroscopy and HRMS. Their spectroscopic properties were analyzed by UV-Vis and fluorescence spectroscopy methods, and production of singlet oxygen ($^1O_2$) by measuring the photodegradation of fluorescent dyes. Antimicrobial activity was assessed on *Pseudomonas aeruginosa* as Gram-negative and *Enterococcus faecalis* as Gram-positive bacteria, in PBS and tap water, without light and under irradiation of violet light (λ = 394 nm, fluence rate 20 mW/cm^2).

Preliminary screening results showed that Zn(II) porphyrin exhibits the strongest inhibition of growth in both bacterial cultures tested, followed by the free-base porphyrin, while the Cu(II) chelated *N*-methylpyridinium-3-yl porphyrin showed the weakest activity. This trend may be related to more efficient production of ROS by the Zn(II) complex due to longer lifetime of the triplet excited state (*PS[3]). [5] Overall, methylated cationic porphyrins showed to be strong candidates as PSs for photoinactivation of opportunistic pathogens.

Acknowlegments: This research was funded by the European Union – NextGenerationEU - METPORPDT - uniri-iz-25-37.

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Nataliia Emashova

Infrared light-based antimicrobial approach

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Most investigations in antimicrobial photodynamic therapy (aPDT) have mainly focused on photosensitizers activated by light in the blue, green, and red spectral regions [1-3]. Indeed, a limited number of studies have explored the potential antimicrobial effects of IR irradiation, either as a standalone treatment or in combination with photosensitizers, indicating a notable gap in current research [3]. Infrared light has an important feature for medicine and veterinary compared to other light-based approaches, namely the depth of light penetration into the tissues up to 10 mm at 700–850 nm [4]. This study evaluates the effect of IR irradiation (combination of two laser sources 905 nm and 808 nm) alone on the viability of four model microorganisms, including Gram-negative Escherichia coli K-12 MG1655 and Pseudomonas aeruginosa PAO1, and Gram-positive Staphylococcus aureus (MSSA) ATCC 25932 and Staphylococcus epidermidis Isolate 4. Moreover, the antimicrobial efficacy of four promising photosensitizers identified during the literature review, namely indocyanine green (ICG), chlorophyll derivatives, Hypericum perforatum extract, and Betadine (povidone-iodine), was investigated against the selected model microorganisms. Two promising photosensitizers demonstrating activity under IR laser irradiation against both Gram-positive and Gram-negative model microorganisms were identified: ICG and Betadine. As a result, it was shown that Gram-negative bacteria were less sensitive to antimicrobial Photodynamic Therapy than Gram-positive ones. The irradiation of Betadine seems to enhance its antimicrobial activity in both Gram-positive and Gram-negative microorganisms. The photo-antimicrobial effect of ICG in E. coli and P. aeruginosa was to delay their growth, while in Gram-positive S. aureus and S. epidermidis was to kill them. Several approaches to enhance the antimicrobial activity of ICG against Gram-negative microorganisms were proposed.

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Chiara Di Donato

Phage platforms for targeted antimicrobial photodynamic therapy

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Bacteriophages have attracted growing interest as scaffolds for biomedical applications, due to their intrinsic biocompatibility and uniform size and morphology. Among them, filamentous M13 bacteriophages stand out for their ease of genetic engineering and ability to carry high payloads of functional molecules, making them an ideal platform for targeted drug delivery.

Building on our previous works demonstrating the efficacy of refactored M13 bacteriophages in photodynamic cancer therapy[1], we extended this strategy to address one of the most critical threats to global public health: antimicrobial resistance. M13 phages were genetically engineered to target different bacterial species by phage-display of peptide targeting moieties fused to the minor coat protein pIII, then, their capsids were chemically functionalized with hundreds of photo-activable Rose Bengal sensitizers. Upon light irradiation, these bioconjugates achieved targeted killing of a range of bacterial pathogens at subnanomolar concentrations[2].

To advance the platform, we incorporated a more efficient thiophene-based photosensitizer[3]. The system was then validated in vivo using Hydra vulgaris as a model organism hosting a Gram-negative–dominated microbiota. M13 phages displaying an LPS-binding peptide on the pIII minor coat protein ($M13_{LPS}$) and a high payload of thiophene-based photosensitizer (TPs) on the pVIII major coat protein ($M13_{LPS}$-TPs) showed, upon controlled light irradiation, selective depletion of Gram-negative bacteria while preserving host integrity and overall microbial equilibrium.

Our findings confirm the synergistic contribution of targeting and photodynamic mechanisms and demonstrate that refactored bacteriophages can serve as modular vectors for minimally invasive, tunable antimicrobial therapies.

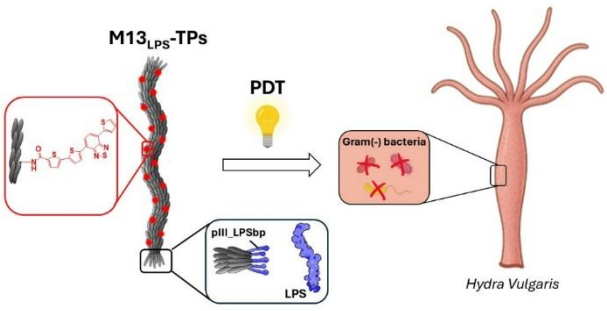


Fig 1. Orthogonal engineering of M13 phage for selective PDT

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Giuseppe Nocito

A photo-antimicrobial hydrogel based on a tetracationic porphyrin and Captisol® assemblies for wound management

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The increasing prevalence of multidrug-resistant pathogens presents a significant challenge in wound infection management, necessitating innovative treatment solutions. In the framework of our research on antimicrobial nanophotosensitizers [1] and hydrogels [2], here we incorporated a supramolecular assembly between a cationic porphyrin (Zinc tetra(4-N-methylpyridyl)porphine tetratosylate – ZnTMPyP) and sulfobutylether β-cyclodextrin (Captisol®) in a bioresorbable hydrogel made of a hyaluronic acid/polylactic acid conjugate (DAC®). Rheology, morphology (SEM, AFM), and erosion profile in physiological medium were assessed. Moreover, the interaction between ZnTMPyP/Captisol assembly and DAC was ascertained by UV/Vis absorption, steady state and time-resolved emission spectroscopies and dynamic light scattering analysis. Photostability was also evaluated. Upon white light irradiation, the eroded hydrogels demonstrated significant photobactericidal activity against both Gram-positive and Gram-negative pathogens, including methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus faecium (VREfm), and Pseudomonas aeruginosa. In darkness conditions, the eroded hydrogels demonstrated negligible antibacterial effects, satisfactory biocompatibility and wound healing potential toward human skin fibroblasts WS1 until 7 and 2 days of treatment, respectively. Overall, samples did not impair and may support cellular migratory capability. Further investigations addressing mechanistic biological aspects would support the therapeutic relevance of the photo-antimicrobial hydrogel based on ZnTMPyP and Captisol as alternative solution to conventional antibiotic treatment for localized wound infection treatment.

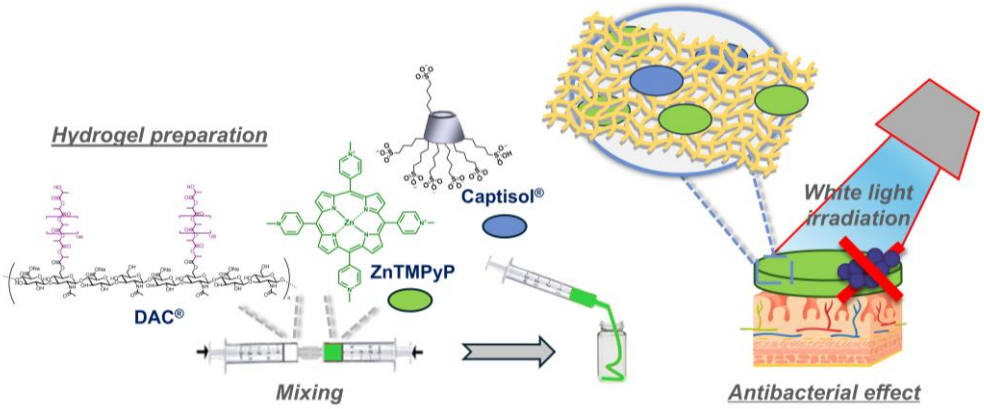


Fig 1. Schematic illustration of hydrogel preparation and photo-antibacterial effect on skin wounds.

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Green-synthesized Prussian blue nanoparticles for synergistic breast cancer therapy

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Research Question: Nanoparticle-based cancer therapy represents an emerging area of research dedicated to the development of more effective and less invasive treatments for oncological patients [1]. This study proposes an innovative synthesis of Prussian blue nanoparticles (PBNPs) for potential breast cancer therapeutic application.

Main Results: To enhance biocompatibility, the synthesis successfully employed pectin extracted from citrus peel as a natural stabilizing and reducing agent, replacing traditional chemical reagents like polyvinylpyrrolidone (PVP). Physicochemical characterization via DLS, TEM, and UV-Vis spectroscopy confirmed the formation of stable, PBNPs. The PBNPs demonstrated high Doxorubicin (Dox) loading efficiency and a good drug release profile. Biological assays (CCK-8) performed on MCF-7 and SKBR-3 breast cancer cell lines demonstrated a significant, dose-dependent reduction in cell viability. TEM analysis confirmed efficient nanoparticle internalization localized within the cytosol. Furthermore, Confocal Laser Scanning Microscopy (CLSM) revealed that Dox-loaded PBNPs significantly altered the organization of the cellular cytoskeleton, corroborating our quantitative data.

Conclusion: Overall, these findings highlight the promising potential of pectin-stabilized PBNPs as innovative and biocompatible therapeutic vectors. Future studies will explore the synergistic effect between drug-loaded PBNPs and photothermal therapy (PTT), as laser-induced hyperthermia is expected to further enhance chemotherapeutic release and cytotoxicity.

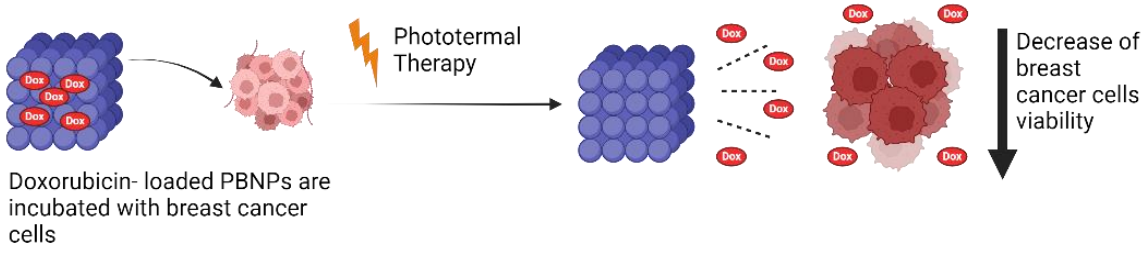


Fig 1. Schematic mechanism of Synergistic Action Between Doxorubicin-Loaded Nanoparticles and Photothermal Therapy.

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Emanuela Peluso

Multilayer of prussian blue nanoparticles with photothermal antibacterial effect

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Research Question. Biofilm-related infections associated with implanted medical devices remain a major clinical challenge due to their high tolerance to antibiotic treatments and their role in surgical site infections. Prussian Blue nanoparticles (PBNPs) are emerging as promising photothermal agents because of their ability to efficiently convert near-infrared (NIR) light into heat. This study investigated the potential of surface-immobilized PBNP multilayers as NIR-responsive antibacterial platforms for the photothermal inactivation of *Staphylococcus aureus* biofilms.

Main Results. PBNPs were successfully assembled as multilayers onto functionalized glass substrates, generating homogeneous coatings with tuneable nanoparticle loading. Surface characterization confirmed the progressive deposition of PBNP layers and their efficient photothermal response under 808 nm NIR irradiation. Upon laser exposure, the functionalized surfaces generated a temperature increase proportional to nanoparticle density. Antibacterial assays performed on *S. aureus* biofilms demonstrated a significant reduction in bacterial viability following NIR irradiation, confirming the effectiveness of the photothermal treatment. The antibacterial activity was further enhanced under experimental conditions that promoted close interactions between bacterial cells and the nanoparticle-coated surfaces.

Conclusion. These findings demonstrate that PBNP multilayers can act as effective NIR-responsive antibacterial surfaces, combining localized photothermal activity with the ability to target bacterial biofilms. The approach offers a promising strategy to address biofilm-associated infections while potentially limiting damage to surrounding tissues. The versatility of PBNPs and their responsiveness to NIR light support their further development as photoactivated antibacterial platforms for biomedical applications and infection control.

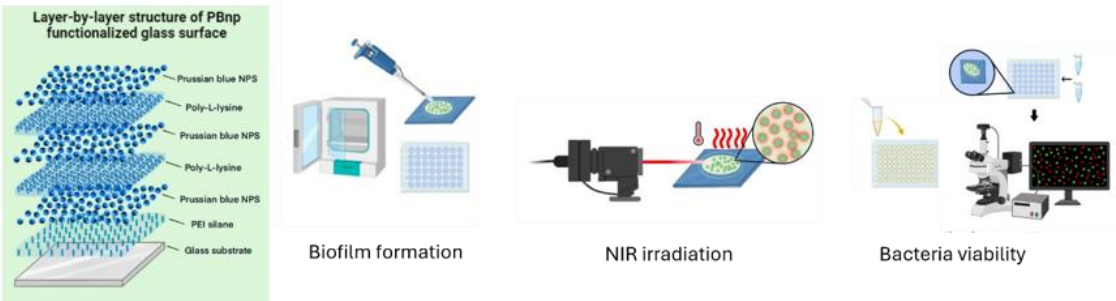


Fig. 1: Schematic mechanism of the photothermal antibacterial effect of PBNPs functionalized glasses.

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Giovanni Romano

Unify, align, and educate: promoting photodynamic inactivation within the One Health framework by COST Action CA24127 PanEuCOPT

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Photodynamic Inactivation (PDI) has gained increasing attention as a valid and effective antimicrobial approach within the One Health framework. This method is based on the photosensitiser-mediated, light-induced overproduction of reactive oxygen species (ROS) in target cells, ultimately leading to the inactivation of a broad range of microorganisms through oxidative mechanisms, independently of their resistance to conventional antimicrobial treatments.

Despite the extensive body of scientific evidence demonstrating the high efficacy of PDI under controlled laboratory conditions, its translation into practical applications remains limited. This is largely due to inconsistent terminology, heterogeneous experimental protocols, and insufficient training and awareness among practitioners in human and veterinary medicine, as well as in environmental sciences and plant protection.

The COST Action CA24127 Pan-European Commission on Photoantimicrobial Testing (PanEuCOPT)[1] brings together more than 150 experts from 28 countries under the shared vision “Unify, Align, and Educate,” with the aim of promoting the standardisation and implementation of PDI in real-world settings. PanEuCOPT is open to researchers, clinicians, and industry professionals from COST and cooperating countries and actively encourages new members to join the initiative.

Within its first year, five dedicated Working Groups have been established: WG1 focuses on terminology standardisation; WG2 advances education and training initiatives; WG3 develops guidelines for testing methods; WG4 defines and harmonises illumination parameters; and WG5 coordinates dissemination and outreach activities.

This presentation provides an overview of PDI, introduces the COST Action, summarises its progress to date, and highlights opportunities for active participation and collaboration within the network.

Acknowledgements: The authors are thankful to COST (European Cooperation in Science and Technology) for supporting this work.

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[1] https://paneucopt.eu

Serena Lembo

Light and skin: photoimmunemodulation

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Photoimmunomodulation refers to the spectrum of local and systemic immune responses induced by solar radiation. As both a physical barrier and a highly specialised immunological organ, the skin continuously interacts with ultraviolet (UV), visible (VIS), and infrared (IR) radiation through endogenous chromophores that convert light energy into molecular and cellular signals. These signals regulate inflammation, immune tolerance, tissue repair, and host defence, influencing both physiological adaptation and disease development. The biological effects of solar radiation depend on wavelength, dose, and tissue penetration. UVB is the principal mediator of epidermal immunomodulation, promoting regulatory immune pathways through DNA damage, cis-urocanic acid formation, vitamin D synthesis, and other immunoregulatory mechanisms. UVA acts predominantly through oxidative stress and reactive oxygen species, contributing to photoaging, immune dysregulation, and photocarcinogenesis (UVA1). In contrast, visible and infrared radiation primarily activate photobiomodulatory pathways involving mitochondrial metabolism and redox signalling, producing dose-dependent effects that range from tissue repair and anti-inflammatory responses to oxidative injury. Photoimmunomodulation involves a complex interaction between structural skin cells, resident and recruited immune cells, melanocytes, dermal adipocytes, neural and vascular components, and cutaneous microbiomes. Together, these elements form an integrated cutaneous ecosystem that dynamically responds to light exposure and shapes both innate and adaptive immune responses. While controlled light exposure can promote immune homeostasis and provides therapeutic benefit, excessive or chronic exposure contributes to immunosenescence, photoaging, photodermatoses, and skin cancer. A better understanding of the cellular and molecular mechanisms underlying photoimmunomodulation is essential for improving photoprotection strategies and for advancing phototherapy and photobiomodulation as targeted approaches for the treatment of immune-mediated and inflammatory skin diseases.