SIFB SYMPOSIUM

BOOK OF ABSTRACTS

Online event on photo-induced processes

Young Researcher Awards

Organized by the Italian Society of Photobiology

7 April, 2025

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PROGRAM

The conference schedule is set to Central European Summer Time (CEST, UTC +2:00)

09:00 Online Platform Opening

09:15 **Greta Varchi** SIFB President

Chair: Sonja Visentin

9:30 **Invited talk by Ardemis Boghossian**, *EPFL, Switzerland*
There's plenty of room for bioengineering optical nanosensors

10:20 **Federica Randisi**, *University of Insubria, Varese, Italy*
Synergistic photodynamic and chemotherapeutic effects using Ce6-encapsulated in folic acid decorated HSA nanoparticles

10:40 **Thomas Lecuyer**, *University of Catania, Italy*
Light activated strategies for cancer treatment

11:00 BREAK

Chair: Valentina Rapozzi

11:20 **Elham Sattarinezhad**, *University of Bologna, Italy*
Exploring the enzymatic mechanism of protochlorophyllide oxidoreductase with molecular dynamics simulations

11:40 **Invited talk by Laura Bellia**, *University of Napoli, Italy*
Lighting and Photobiology: the CIE role

12:10 **Invited talk by Giuseppe Paternò**, *Polytechnic of Milan, Italy*
Phototaming of bacterial bioelectricity

13:00 BREAK

Chair: Rossella Labarile

14:00 **Invited talk by Santi Nonell Marrugat**, *Ramon Llull University, Spain*
Light and life: a chemist turned photobiologist. A miscelanea of highlights of my research career – and lessons learned along the way

14:50 **YRA Alessio Colleoni**
Modulation of bacterial cell adhesion proteins via photoswitchable ligands: a promising strategy to counteract biofilm formation

15:00 **YRA Francesca Bianco**
NIR pH-responsive PEGylated PLGA nanoparticles as effective phototoxic agents in resistant PDAC cells

15:10 **YRA Chiara Florindi**
Amphiphilic membrane-targeted phototransducers for non-genetic optical stimulation of cellular bioelectricity

15:20 **YRA Alessia Lena**
Application of blue light for the inactivation of planktonic and biofilm forms of *Listeria monocytogenes*

15:30 **YRA Benjamin Clepoint**
"Green" gold nanostructures for photothermal and photodynamic therapies

15:40 **YRA Asja Brovedani**
Vanillin-based materials for photoactivated antimicrobial applications

15:50 BREAK

Chair: Marzia Gariboldi

16:10 **YRA David Grantz**
Fully reversible control over DNA-intercalation with visible light

16:20 **YRA Michela Nigro**
A newly designed phage-based nanobot for precision photodynamic and sonodynamic cancer therapy

16:30 **YRA Claudia Zonno**
Effects of deep eutectic solvents on the stability of chromatophores from *Rhodobacter sphaeroides*

16:40 **YRA Manuele Di Sante**
Regenerative efficacy of biocompatible carbon nanoheaters

16:50 **YRA Andrea Martino**
M13 phage-based nanovectors as a phototheranostic platform for the treatment of ovarian cancer

17:00 **Nayeli Fernanda Perez-Perez**, *Barcelona Institute of Science and Technology, Spain*
Photocontrol of behavior with photoswitchable ligands of α7 nicotinic acetylcholine receptors

17:20 BREAK

17:30 **Announcement of the Young Researcher Awards (YRA)**

Federica Randisi

Synergistic photodynamic and chemotherapeutic effects using Ce6-encapsulated in folic acid decorated HSA nanoparticles

Federica Randisi[1], Claudia Ferroni[2], Andrea Guerrini[2], Emanuela Marras[1], Greta Varchi[2], Marzia B. Gariboldi[1].

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Photodynamic therapy (PDT) has gained recognition as a promising oncologic treatment modality due to its relatively low systemic toxicity, absence of resistance induction, and minimal invasiveness. This therapeutic approach relies on the interaction between a photosensitizer (PS), light, and molecular oxygen to generate reactive oxygen species (ROS), which induce oxidative stress-mediated cytotoxicity in malignant cells. Chlorin e6 (Ce6), a widely utilized PS in PDT, possesses advantageous physicochemical and photobiological characteristics, including strong absorption in the red region of the visible spectrum (~ 660 nm), enabling deep tissue penetration, and high photoconversion efficiency, a crucial determinant of effective photodynamic cytotoxicity. However, Ce6 exhibits poor aqueous solubility, and tends to aggregate in physiological environments, resulting in self-quenching of its excited states, thereby compromising ROS generation and overall photodynamic efficacy. Furthermore, Ce6 suffers from suboptimal tumor accumulation, limited biodistribution, and a short systemic circulation half-life, which collectively hinder its therapeutic potential. Moreover, the effectiveness of PDT, regardless of the PS used, is significantly reduced by the hypoxic conditions common in solid tumors, highlighting the need for innovative strategies to improve treatment results. To address these challenges, various studies have focused on improving the pharmacological profile of Ce6 through bioconjugation with targeting ligands to enhance specificity and cellular uptake, as well as incorporation into nano-based delivery systems to improve solubility and stability in biological environments. Nanoparticle formulations have emerged as a promising approach for therapeutic protection and targeted delivery, leveraging the versatile properties of protein-based and hybrid drug carriers composed of proteins and synthetic polymers. Albumin exhibits several advantageous properties, including biocompatibility, high biodegradability with safe metabolic byproducts, water solubility, and low immunogenicity. Additionally, albumin nanoparticles possess multiple drug-binding sites, facilitating increased drug-loading capacity.

The specificity of nano-based delivery systems can be further enhanced through their functionalization with ligands that selectively bind to receptors known to be overexpressed in cancer cells, such as the epidermal growth factor receptor (EGFR) and the folic acid receptor (FR). This targeted approach facilitates improved cellular uptake and therapeutic efficacy by exploiting receptor-mediated endocytosis mechanisms. Moreover, extensive research has demonstrated that the combination of a PS with conventional chemotherapeutic agents, such as doxorubicin and paclitaxel (PTX), in both free and nano-formulated states, can produce synergistic effects. This highlights the potential of combination therapies to improve anticancer outcomes through enhanced cytotoxicity and therapeutic selectivity.

In this work, a novel human serum albumin (HSA) hybrid nanoparticle in which the high affinity of the phospholipidic part of DSPE-PEG hybrid decorated with folic acid (DSPE-PEG-FA) for HSA was exploited for binding it in a non-covalent manner, without modifying its structure. This method exponentially increases the loading capacity of pro-drugs/drugs in the complex with HSA. The complex was then used to encapsulate Ce6, and a bioresponsive PTX dimeric prodrug (PXT-PTX), and tested as PS for PDT on two lung cancer cell lines exhibiting differential expression levels of FR. We evaluated their cytotoxic effect, along with cellular uptake, ROS, and singlet oxygen generation, and their ability to induce apoptotic cell death. Our findings revealed a synergistic interaction between Ce6 and PTX-PTX in the formulations, leading to a

significantly enhanced cytotoxic effect compared to free Ce6 and PTX-PTX, likely due to improved cellular accumulation mainly in the cell line overexpressing FR, as evaluated through flow cytometric analysis of cells incubated with free and HSA formulations. Furthermore, substantial ROS and singlet oxygen production resulted in pronounced apoptotic cell death. As expected, when PDT effects on cell viability were assessed under hypoxic conditions, the efficacy of all tested compounds was markedly attenuated. To overcome this limitation, we incorporated MnO_2, a well-established oxygen-generating agent, into the formulation. These modified nanoparticles exhibited comparable photodynamic efficacy under both normoxic and hypoxic conditions, highlighting their potential for conquering tumor hypoxia-associated PDT resistance.

Thomas Lécuyer

Light activated strategies for cancer treatment

Thomas Lécuyer[1], Serena Silvi[2], Aurore Fraix [1]

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In the context of low turnover of new drugs and need for the development of personal medicine, there is an urgent call for alternative smart therapeutic strategies. In this setting, light provides exciting perspectives offering the unique opportunity to play with controlled release of conventional drug or generation of unconventional active species (e.g. heat, reactive oxygen species, reactive nitrogen species).

Donor-Acceptor Stenhouse Adducts (DASA) are a new family of photochromes that lately gains more and more attention into the scientific community. These compounds present a ground-breaking property: switching from an open-coloured form to a closed-colourless form with low energy visible-light excitation, their polarity also change, from apolar to polar [1]. This uncommon property opens the way for multiple applications of these new photochromes, such as photo-switch for controlled drug delivery.

Although some properties of DASAs in organic solvents have already been described, their behaviour in aqueous solution [2] and furthermore their use in biocompatible nanostructure still need to be explored.

Moreover, ad hoc modified DASAs can be good candidate for the release of active specie in the specific hypoxic conditions often encounter in the tumour environment.

In this contribution we will focus on a formulation of DASAs in liposome and the behaviour of this system under light irradiation.

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Elham Sattarinezhad

Exploring the Mechanism of Protochlorophyllide to Chlorophyllide Conversion

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During light-driven chlorophyll biosynthesis, protochlorophyllide (Pchlide) is reduced to chlorophyllide by protochlorophyllide oxidoreductase (POR) in the presence of the ubiquitous nicotinamide adenine dinucleotide phosphate (NADPH) cofactor. This process is essential for plant development and offers a unique opportunity to investigate enzymatic catalysis occurring atlow temperatures and on an ultrafast timescale [1] **(Fig.1)**.

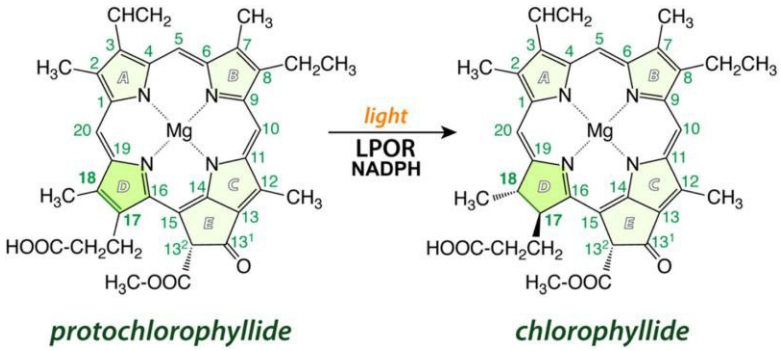

Fig.1. A scheme of the reaction catalyzed by LPOR

Despite several proposed models, the precise orientation of Pchlide in the active site remains unresolved, limiting our understanding of the reaction mechanism. In this work, we combined recent structural data from crystallography and electron microscopy (cryo-EM) with funnel well-tempered metadynamics simulations to determine the most favorable orientation of Pchlide in theactive site of POR. Our results reveal a stable binding conformation that supports efficient hydride transfer, providing key insights into the initial steps of Pchlide reduction.

This study establishes a structural foundation for further mechanistic investigations, sheddinglight on the intricate photochemical conversion essential for chlorophyll biosynthesis.

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Nayeli Fernanda Pérez-Pérez

Photocontrol of behavior with photoswitchable ligands of α7 nicotinic acetylcholine receptors

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The α7 nicotinic acetylcholine receptor (α7 nAChR) is a key modulator of cognitive function, inflammation, and neuronal signaling, making it an attractive therapeutic target for neurodegenerative and neuropsychiatric disorders. However, traditional pharmacological interventions lack precise spatial and temporal control, often leading to off-target effects. Photopharmacology offers a novel approach to modulate α7 nAChRs with high precision.

Here, we present the design, synthesis, and functional characterization of a novel photoswitchable α7 ligand, CPZ-2. Rationally designed through azologization, CPZ-2 exhibits reversible photoisomerization, achieving efficient trans-to-cis conversion under 380 nm light and reversal at 430 nm. The ligand demonstrated photostability, slow thermal relaxation, and potential for two-photon activation, enabling deep-tissue applications. Radioligand binding assays confirmed α7 receptor selectivity, while behavioral assays in zebrafish larvae revealed the ability of CPZ-2 to modulate nicotine-induced locomotion in a light-dependent manner.

Our findings establish CPZ-2 as a promising tool for optically controlled α7 nAChR modulation, with potential applications in neuroscience, inflammation, and pain research. Further studies will explore its utility in circuit dissection and therapeutic interventions.

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Alessio Colleoni

Modulation of bacterial cell adhesion proteins via photoswitchable ligand: a promising strategy to counteract biofilm formation

Alessio Colleoni[1,2], Giorgia Tempra[1], Shapla Bhattacharya[3,4], Marco De Amici[1], Rossella Castagna[3,5], Emilio Parisini[3,6], Carlo Matera[1]

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Antimicrobial resistance (AMR) is an escalating global threat, posing a critical challenge to modern medicine, particularly in the context of nosocomial infections. Among the various factors driving the spread of AMR, biofilm formation represents a major contributor, as it provides a protective niche for pathogens and facilitates the horizontal transfer of resistance genes across species [1]. Central to biofilm formation are bacterial cell adhesion proteins, which mediate cell-to-cell and cell-to-surface interactions, enabling the development of dense microbial communities that exhibit heightened resistance to antimicrobial agents. Given their pivotal role in biofilm formation, adhesion proteins represent ever-increasing attractive therapeutic targets for the treatment of AMR. Among the different potential adhesion proteins target, bacteria Virulence Factor (LecB) protein, a bacterial outer-membrane protein of *Pseudomonas aeruginosa* (a notable gram-negative pathogen causing hospital-acquired infections), aroused interest both for the major threat of this strain to current and future healthcare worldwide and for its ability to bind carbohydrate moieties in the *P. aeruginosa* outer membrane as well as exopolysaccharides in the biofilm matrix [2,3].

Considering what mentioned before, this project aims at identifying and developing novel photoswitchable ligands capable of binding to and modulating the activity of LecB protein for the treatment of AMR. By leveraging light-activated protocols, these ligands could offer a promising alternative to conventional antimicrobials, providing a non-invasive approach with precise spatial and temporal control. The design strategy, the chemical synthesis and the proper photochemical characterization as well as the preliminary biological evaluation will be presented and discussed.

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Francesca Bianco

NIR pH-responsive PEGylated PLGA nanoparticles as effective phototoxic agents in resistantPDAC cells

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Pancreatic Ductal Adenocarcinoma (PDAC) is characterized by a tumor microenvironment (TME) formed by cancerassociated fibroblasts (CAFs) and pancreatic stromal cells (PSCs) secretions, creating a dense matrix, which makes difficult for nutrients and oxygen to diffuse [1]. Therefore, the tumor core becomes hypoxic and acidic [2,3], which promotes the selection of cellular clones characterized by increased aggressiveness and resistance against chemotherapy and the expression of epithelial-to-mesenchymal transition (EMT) markers [4,5]. Surgery is the majortreatment, as well as chemotherapy, using FOLFIRINOX (5-fluorouracil, leucovorin, irinotecan, and oxaliplatin) or gemcitabine-based therapies [6,7].

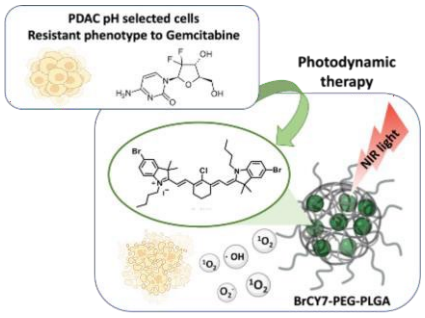

Fig. 1. Graphical abstract

Photodynamic therapy (PDT) is a minimally invasive treatment, applied also in cancer therapy [8], based on the administration of a photosensitizer (PS), which localizes in tumor cells, the area is locally irradiated, causing the molecule activation and so cancer cell death [9]. Among the different classes of PS, the PMDs have been characterized in our laboratories [10,11] as promising candidates as PS. Cyanines dyes (CYs) show excellent photophysical and photochemical properties such as sharp and intense absorption bands and narrow emission bands with high extinction coefficients in the red and NIR, high fluorescence quantum yield and low dark toxicity [12]. Their limited solubility results in compromised photochemical properties, with a consequent altered PDT effect. To address these limitations, we loaded them into PEG-ylated poly lactic-co-glycolic acid (PLGA). We proposed an alternative treatment for chemotherapy-resistant PDAC, characterizing a bromine substituted indolenine-based heptamethine-cyanine dye (BrCY7), which absorbs in the NIR (795nm), loaded into PEG-PLGA nanoparticles, and administered to PANC-1 cell lines. To mimic PDAC TME, we previously characterized PANC-1 CT,maintained in pH_e 7.4, instead PANC-1 pH selected are maintained for 30 days at pH_e 6.6 [13]. We demonstrated that our cells tolerate the BrCY7-PEG-PLGA up to 2 µM and when the cells treated are photoactivated PANC-1 pH selected viability has been significantly reduced, more than the ones treated with gemcitabine (first line chemotherapeutic drug against PDAC). On

the contrary, BrCY7-PEG-PLGA does not have any effect on PANC-1 CT, suggesting a possible pH dependent degradation of the PEG-PLGA nanoparticles.

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Chiara Florindi

Amphiphilic membrane-targeted phototransducers for non-genetic optical stimulation of cellular bioelectricity

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The use of light to modulate cellular activity is emerging as a powerful and versatile tool in cell biology, offering minimal invasiveness, unparalleled spatiotemporal precision, and reversibility, thereby surpassing traditional stimulation methods.

While optogenetics has significantly advanced the field, its clinical application faces challenges related to delivery, safety, biocompatibility, and ethical concerns.

In contrast, non-genetic photostimulation is an increasingly prominent and multidisciplinary approach aimed at inducing light sensitivity in living systems using exogenous phototransducers.[1]

In this context, we present two recently synthesized intramembrane azobenzene photoswitches, Ziapin2 and MTP2, as potential candidates for optically modulating the electrical properties of excitable cells. Both compounds integrate into the plasma membrane and modulate the membrane potential (V_m) without forming covalent interactions or directly altering ionic conductance. Notably, Ziapin2 induces mechanical photomodulation, resulting in a transient hyperpolarization followed by a delayed depolarization, which is sufficient to trigger action potential generation in excitable cells.[2,3,4] Conversely, MTP2 induces electrical photomodulation, resulting in a sub-threshold depolarization, which is highly dependent on light intensity.[5]

Together, these findings provide proof of concept that Ziapin2 and MTP2 represent promising tools for the geneless optomodulation of cellular electrical behavior, opening interesting perspectives for a wide range of applications.

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Alessia Lena

Application of Blue Light for the inactivation of planktonic and biofilm forms of *Listeria monocytogenes*

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Blue Light (BL) technology has emerged as a promising microbial inactivation method due to its safety, cost-effectiveness, and sustainability. BL operates by activating photosensitizers (PS), which generate reactive oxygen species (ROS) that damage microbial cells, leading to their inactivation [1]. While its efficacy has been widely demonstrated against medically relevant bacteria, recent studies have focused on its potential application in food safety, particularly for inactivating *Listeria monocytogenes*, a persistent foodborne pathogen [2, 3].

This study investigated the effects of BL at three wavelengths (in the range 405- 450 nm) on *L. monocytogenes* in both planktonic and biofilm states. Higher BL doses (300–700 J cm^{-2}) successfully inactivated planktonic cells but also generated excessive heat dissipation, while lower doses (<300 J cm^{-2}) resulted in varied inactivation levels depending on the wavelength. In solution, 405 nm was the most effective, although inactivation was lower compared to agar-based experiments, probably due to the nature of the substrate [4].

For biofilms, 5-day biofilm treatment showed similar reductions across all wavelengths, with 405 nm achieving the highest inactivation. However, in 13-day biofilms, lower BL wavelengths performed similarly, as confirmed by CLSM, which also revealed structural modifications such as elongated cell morphology, indicated stress responses, suggesting an adaptive response to BL-induced stress [5].

These findings highlight BL's potential use in food-related environment but emphasize the need for optimization of parameters such as light dose, wavelength, and substrate characteristics for effective microbial control.

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Benjamin Clepoint

"Green" Gold Nanostructures for Photothermal and Photodynamic Therapies

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The low turnover of new anticancer drugs and the rising antimicrobial resistance call for an urgent shift of attention to unconventional medicines. Photothermal and photodynamic therapies uses respectively controlled heat and singlet oxygen releases, which are localized and can interact with multiple targets, generated under light stimulation for precise treatment control. Gold nanoparticles (AuNPs) are promising for both therapies against cancer and bacteria drug resistance.[1] There is a lack of reports on the green synthesis of anisotropic AuNPs, which are essential for *in vivo* applications.[2]

Two nanoscale systems were explored using curcumin and indigo carmine as green reducing agents. A b-cyclodextrin polymer was used as a templating and stabilizing agent, to enhance the solubility of the reducing agents and as carrier of THPP used as a photosensitizer. The characterization of gold nanostructures and their photothermal and photodynamic properties were performed when possible. UV-Vis absorbance spectra of both systems demonstrated the characteristic band of anisotropic AuNPs in near-infrared region. With an irradiation in the latter, the curcumin-reduced system exhibited a repeatable temperature increase of 14-15°C and in the blue region a singlet oxygen production. TEM images revealed prism and worm-like shapes. While the indigo carmine-reduced system showed a 6-12°C temperature increase (Fig. 1). Both gold nanostructures demonstrate very promising results for anticancer and antimicrobial drug resistance.

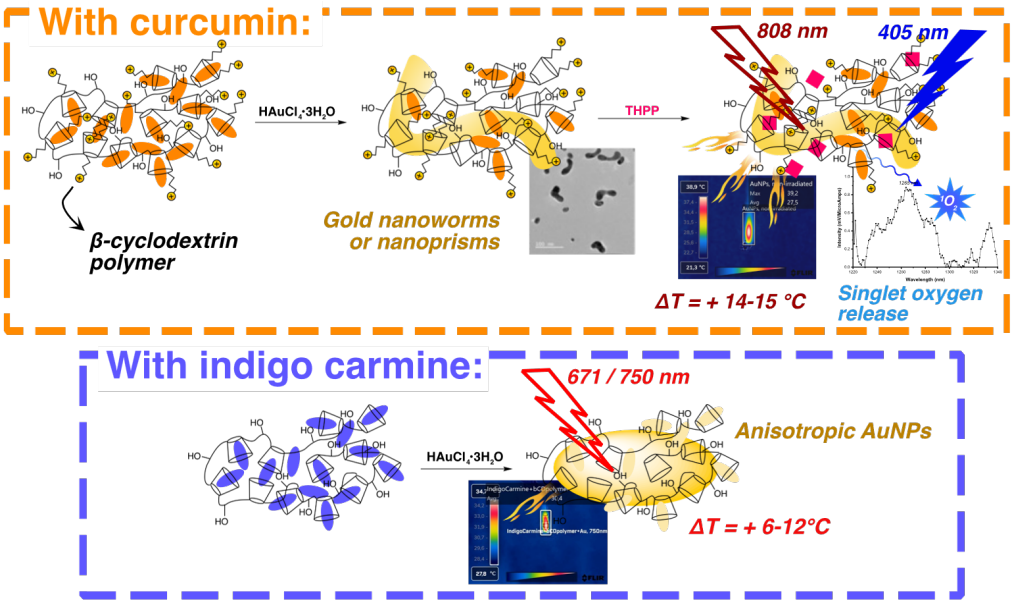

Fig. 1. Synthesis of the gold nanoparticle from $HAuCl_4 \bullet 3H_2O$ reduced by curcumin or indigo carmine. The gold nanosystem is then irradiated in near-infrared region for heating investigation and in the blue region for $^1O_2$ production.

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Asja Brovedani

Vanillin-Based Materials for Photoactivated Antimicrobial Applications

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The growing threat of antibiotic resistance demands innovative strategies to address the "superbug" challenge and combat harmful microorganisms. One promising approach is using antimicrobial materials, which are increasingly promoted as an effective means to limit the spread of pathogens [1]. A key strategy involves bacteria eradication via oxidative stress induced by exogenous reactive oxygen species (ROS). As a result, ROS-generating materials are gaining attention as disinfection agents [2].

Among these, photoactivable materials used in photodynamic inactivation (PDI) stand out as a particularly interesting class. PDI employs light to activate oxygen, converting it into an antimicrobial agent through a photoactive molecule known as a photosensitizer (PS) [3]. PDI-active materials can be developed either by polymerizing PS agents directly or by immobilizing PS on a suitable support, often using polymeric matrices. To enhance environmental sustainability, biomolecules derived from biomass offer valuable potential for designing innovative, biobased supports with antimicrobial properties [4].

This study reports the synthesis and complete physical, chemical, and biological characterization of new materials derived from biomolecules obtained from lignin with or without including a PS.

Experimental results demonstrated that exposing 1 cm^2 of the material to blue light at a fluence rate of 100 W/m^2 within 90 minutes reduced the initial S. aureus load (10^7 CFU/ml) to up to 4log. Additionally, the potential for reusing these materials was explored, with findings indicating that photodynamic activity improved in some cases over successive disinfection cycles.

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David Grantz

Fully reversible control over DNA-intercalation with visible light

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DNA-binding agents are widely used chemotherapeutics in cancer therapy. Many established drugs, such as Cisplatin, share one intrinsic obstacle, the treatment comes with severe side-effects due to low specificity [1]. This prevalent problem in cancer therapy can be mitigated by employing the emerging concept of Photopharmacology, where the activity of a drug can be spatiotemporally controlled by the use of non-harmful visible light.

We introduce Diazocine photoswitches (cyclic Azobenzenes) as a promising scaffold for reversible DNA-intercalation in photopharmacological cancer therapy. Diazocines are stable in *cis*-configuration and can be isomerized to *trans*-configuration by the use of blue light (400 nm). The metastable *trans*-Isomer can revert to the *cis*-state thermally or by irradiation with green light (535 nm). The difference in DNA binding behaviour can be explained by the change in geometry upon switching. While the flat *trans*-Isomer can intercalate between the base pairs, the sterically demanding, angled *cis*-Isomer is expelled from the DNA-Diazocine complex.

In our study, we synthesized a library of potential Diazocine based DNA-intercalators based on the results of Molecular Dynamics screening. All molecules were photochemically characterized under physiological conditions and the binding to genomic DNA was assessed with Circular-Dichroism Spectroscopy.

Our compounds show full reversibility of DNA-Binding upon irradiation, and could do so without fatigue for at least 5 cycles.

The large change in affinity combined with the near-quantitative photoconversion of the Diazocines isomers lead to highly selective binding and unbinding over a wide concentration range, promising better targeting for chemotherapeutics.

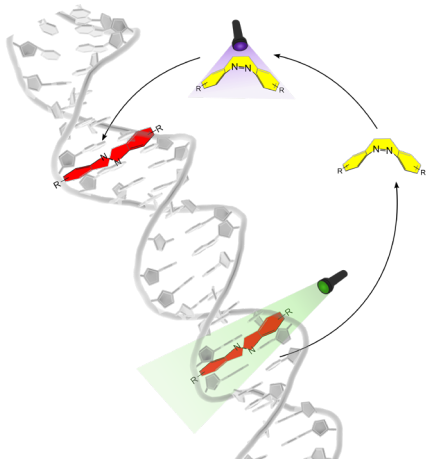

Fig. 1. Schematic representation of visible light triggered reversible intercalation and deintercalation from DNA of Diazocine

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Michela Nigro

A newly designed phage-based nanobot for precision photodynamic and sonodynamic cancertherapy

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Photodynamic and Sonodynamic Therapy (PDT/SDT) are emerging non-invasive approaches to cancer treatment based on molecules known as sensitizers that, when activated by light or ultrasound, generate reactive oxygen species (ROS) leading to tumour ablation. However, low accumulation of sensitizers in the tumour mass has significantly reduced the therapeutic potential of PDT/SDT. This study explores the potential use of M13 bacteriophages as targeted nanovectors for selective photo and sonodynamic eradication of cancer cells.

M13 phages were genetically modified to display the 7D12 nanobody, specific for the Epidermal Growth Factor Receptor (EGFR), which is overexpressed in several type of cancer. The capsid of the engineered $M13_{7D12}$ phage was further functionalized with fluorophores, enabling selective targeting of EGFR-overexpressing A431 cells while minimizing interaction with EGFR-negative controls.

Additionally, M137D12 was chemically conjugated with Rose Bengal (RB), a well-characterized sensitizer, onto the pVIII major coat proteins, generating $M13_{7D12}$-RB (Fig.1A) nanovectors capable of delivering hundreds of RB molecules per phage particle. $M13_{7D12}$-RB exhibited potent and selective photo and sonodynamic cytotoxicity in 2Dand 3D tumour models (Fig. 1F), leading to significant tumour spheroid disruption. Notably, ex vivo analysis confirmed deep tumour penetration and complete disaggregation of the spheroid architecture following light or ultrasound exposure.

To conclude, the engineered $M13_{7D12}$-RB nanovector represents a promising platform for targeted PDT and SDT. Itsremarkable specificity, efficient tumour penetration and potent activated cytotoxicity highlight its potential as an innovative and versatile strategy for treating treatment-resistant malignancies. These attributes underscore the suitability of phage-based nanovectors as a scalable and adaptable approach for precision oncology applications.

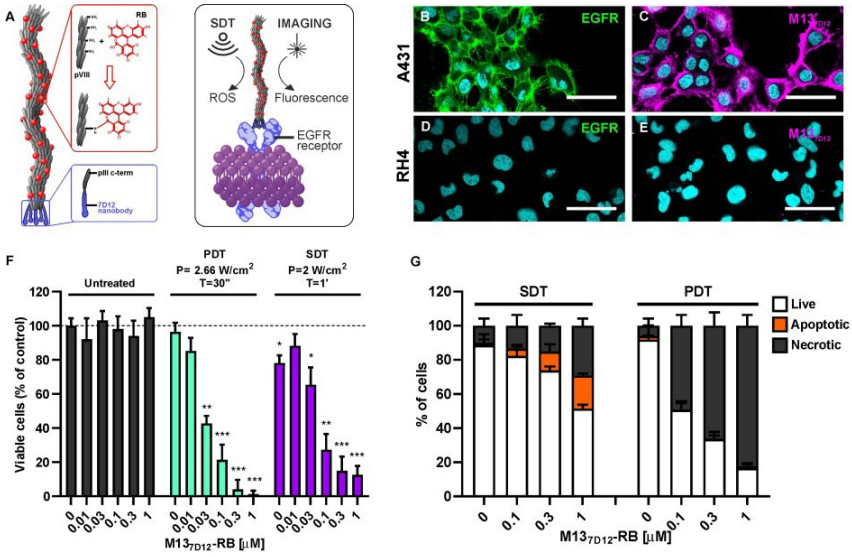

Fig. 1. Phage modification scheme and $M13_{7D12}$ targets EGFR positive cells (**A**). EGFR expression (**B, D**) and targeting of M137D12 (**C, E**) on A431 (**B, C**) and RH4 (**D, E**) cell lines. M137D12-RB tumor ablation was evaluated in vitro (**F**) on A431 cell line. FACS analysis of the mechanisms of death on the on the A431 cell line (**G**).

Claudia Zonno

Effects of Deep Eutectic Solvents on the stability of chromatophores from *Rhodobacter sphaeroides*

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Deep eutectic solvents (DES) are innovative sustainable solvents characterized by melting points much lower than those of individual components[1]. The decrease in the melting point of the mixture is due to a strong interaction between the components, leading to a less ordered structure that maintains them liquid at room temperature and sustains chemical stability of molecules that are solved into. Most DES are not toxic, generally low-cost, and their preparation is easy and straightforward. Thus, little or no waste is generated in chemical synthesis and no purification is required.

DESs have been shown to maintain the catalytic activity of the membrane photosynthetic enzyme – known as reaction center (RC) – obtained from the purple non sulphur bacterium from *Rhodobacter sphaeroides*. Nine different DESs were tested and all but one showed full compatibility with the membrane protein[2].

In this study, we widened our investigation to evaluate the compatibility of DESs toward photosynthetic membrane vesicles cointaining RC and light-harvesting complexes called chromatophores, isolated from the mutant strain R26 of R. *sphaeroides*. Three different DESs were studied, namely TBAB:Gly (1:3), ChCl:EG (1:3) and ChCl:U (1:2) and their effect on the integrity of vesicles was analysed by UV-Vis-NIR spectroscopy.

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Keywords*: DES, soluble protein, membrane protein, photosyntetic system*

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Manuele Di Sante

Regenerative efficacy of biocompatible carbon nanoheaters

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The local delivery of a low heat dose can be exploited in regenerative medicine, augmenting tissue regeneration. Carbon Nanotubes (CNTs) efficiently convert near infrared radiation (NIR) into heat and are under extensive investigation because of their potential as intracellular nanoheaters [1]. However, the use of CNTs in biological systems still presents important restrictions due to 1) low biocompatibility; 2) dependency of their properties and toxicity on the physiological environment and 3) the related aggregation phenomena.
Proteins can be used to disperse efficiently in water CNTs with a "green" supramolecular approach, minimizing undesirable toxic responses and controlling their biodistribution/cellular uptake [2].
Here we synthesized various CNT-protein hybrids using lysozyme and bovine serum albumin as model proteins and different sized CNTs (CNT(6,5) or CoMoCAT). The protein platform offered different chemical groups for an easy route of functionalization of the hybrids (figure 1), that were engineered by cationization (using cationizing agents such as ethylenediamine), or covalently linking targeting agents (i.e. EGF protein) and/or fluorescent tags (i.e. Fluorescein isothiocyanate) [3].

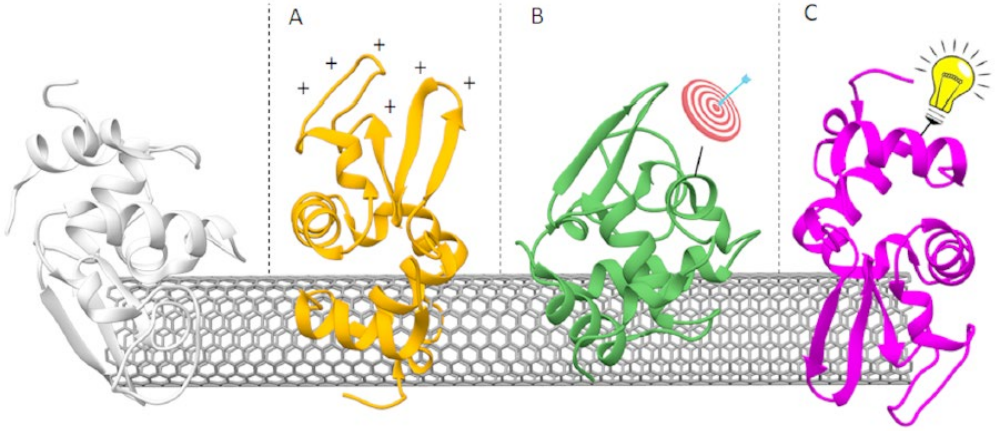

Fig. 1. Engineering of CNT-Protein hybrids by cationization (A), bioconjugation of targeting agents (B) or fluorescent tags (C).

The stability of the nano-hybrids in different media was assessed, and their heating ability was measured upon NIR-irradiation. *Hydra vulgaris* was used as an *in vivo* model, due to its capability of regenerating the complete individual from amputated body parts, to demonstrate the efficacy of the nanoplatform in regenerative medicine.

Acknowledgment: Funded by the European Union – NextGenerationEU, Phoenix: Enhancing tissue regeneration through carbon nanoheaters, P2022LE4BE, CUP B53D23031710001.

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Andrea Martino

M13 phage-based nanovectors as a phototheranostic platform for the treatment of ovariancancer

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Ovarian cancer (OC) is one of the leading causes of cancer-related deaths due to its asymptomatic progression, which often results in a late-stage diagnosis and significantly reduced survival rates. A major challenge in early detection is the lack of effective biomarkers for detecting early-stage OC. Although the combination of debulking surgery and chemotherapy has substantially improved treatment outcomes, chemotherapy resistance remains a significant cause of recurrence in OC patients. To address these challenges, combining different therapeutic modalities may offer more effective treatment strategies[1].

OC cells frequently exhibit an overexpression of folate receptor alpha (FRα), making it an attractive target for anticancer therapies. Photodynamic therapy (PDT) is a clinically approved, minimally invasive approach characterized by its high spatial selectivity for target tissue, making it a promising candidate for localized treatment.

This work is part of the "PhageLight" project, which aims to develop innovative targeted phototeranostic platforms for OC treatment. Using phage display technology, a refactored M13 phage targeting FRα was engineered and utilized as a platform. The major coat protein of the viral capsid was chemically modified to incorporate both fluorophores, serving as imaging probes, and standard photosensitizers for PDT[2].

In this research pitch session, I will present the synthesis, purification and characterization strategies employed for these phage-based bioconjugates, as well as their in vitro evaluation as phototheranostic agents for OC treatment.

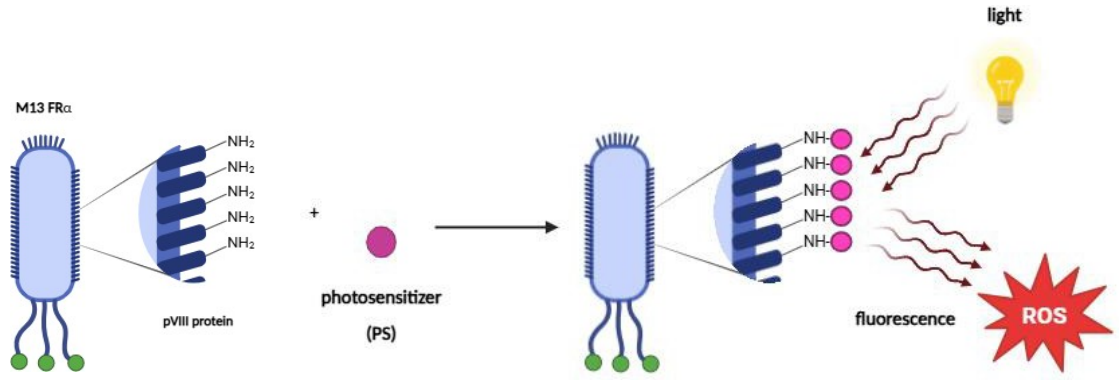

Fig. 1. Schematic representation of the aim of this project

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