Italian Society of Photobiology XXXIV Annual Conference

Sala Conferenze del Rettorato **Lecce 28 – 30 June 2023**

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Conference Program

Conference keywords
Photobiology and Biophysics at the nanoscale
Light -responsive materials
In vitro photodynamic investigations: focus on antimicrobial strategies
In vitro photodynamic investigations: focus on antitumoral strategies

Wednesday 28 June 2023	
14:30 - 15:00	**REGISTRATION**
15:00 - 15:30	**OPENINGS**
15:30 - 16:00	**Sabrina Conoci** *"Ultrasensitive PCR- Free Biosensors Based on Photonics Transduction"*
16:00 - 16:20	**Tainah Dorina_Marforio** *"Designing phototheranostic platforms by in silico approach"*
16:20 - 16:40	**Giulia Giugliano** *"Identification by virtual screening of fullerene carrier proteins for PDT applications"*
16:40 - 17:10	**COFFEE BREAK**
17:10 - 17:30	**Sofia Leo** *"The radiotherapeutic effects of photosensitizers: An overview of the physical, chemical, and biological mechanisms"*
17:30 - 17:50	**Edoardo Jun_Mattioli** *"Identification of Blood Transport Proteins to Carry Temoporfin: A Domino Approach from Virtual Screening to Synthesis and In Vitro PDT Testing"*
17:50 - 18:10	**Sonja Visentin** *"Mucins as potential biomarkers for early detection of cancer and as drug delivery systems for PDT"*
18:10 - 19:30	**SIFB meeting with elections**
Thursday 29 June 2023	
9:00 - 9:30	**Jenny Zhang** *"Stealing electrons from photosynthesis"*
9:30 - 9:50	**Maya Dimova Lambreva** *"Photosystem II electron transport rerouted by single-walled carbon nanotubes"*
9:50 - 10:10	**Cesar Vicente-Garcia** *"Diatom Microalgae as Promising Candidates for the Construction of Robust Biophotovoltaic Devices"*
10:10: 10:30	**Maria Varsalona** *"Interaction between Rhodobacter sphaeroides and polydopamine: efficiency of both photosynthetic growth and polymerization"*
10:30 - 10:50	**Giacomo Mandriota** *"Winogradsky column as tool for microbial communities enrichment"*
10:50 - 11:20	COFFEE BREAK
11:20 - 11:40	**Rossella Labarile** *"Coffee-based photoelectrochemical system with Rhodobacter sphaeroides"*
11:40 - 11:45	**YOUNG INVESTIGATORS AWARD**
11:45 - 12:10	**Gabriella Buscemi** *"Bio-Inspired Redox-Adhesive Polydopamine Matrix for Intact Bacteria Biohybrid Photoanodes"*
12:10 - 12:35	**Giorgia Chinigò** *"Polymethine dyes-loaded solid lipid nanoparticles (SLN) as promising photosensitizers for biomedical applications"*
12:35 - 14:00	LUNCH BREAK - Poster session
14:00 - 14:30	**Mans Broekgaarden** *"Spatiotemporal controlled drug delivery with light- and radiotherapy-responsive liposomes"*
14:30 - 14:50	**Roberto Saporetti** *"Nanoarchitectonics of the M13 phage provides a potent and specific anti-GD2 vector platform for Neuroblastoma Therapy"*
14:50 - 15:10	**Matteo Calvaresi** *"NanoPhages: Photoactive bacteriophages for receptor targeted PDT"*
15:10 - 15:30	**Paolo Emidio Costantini** *"A modular phage vector platform for targeted photodynamic therapy of Gram-negative bacterial pathogens"*
15:30 - 15:50	**Maria Alexandra Cucu** *"Photoinactivation of Pseudomonas aeruginosa and Staphylococcus aureus biofilm by a non-uniform LED illumination method"*

15:50 - 16:20	**COFFEE BREAK**
16:20 - 16:50	**Valérie Heitz** *"Targeting the Near-Infrared: π-Extended Conjugates for Photodynamic Therapy and Theranostic Applications"*
16:50 - 17:10	**Alessia Marconi** *"Human Serum Albumin: an effective drug delivery system for photodynamic therapy"*
17:10 - 17:30	**Mariachiara Gani** *"Can photodynamic therapy treatment overcome drug resistance in pancreatic cancer cells?"*
17:30 - 17:50	**Elisa Martella** *"Mesenchymal Stromal cells as active carriers of chemo and photodynamic therapy-based nanoparticles for osteosarcoma treatment"*
17:50 - 18:10	**Miryam Chiara Malacarne** *"Evaluation of nanoparticles covalently bound with a BODIPY for their possible PDT applicability"*
20:30	**SOCIAL DINNER**
Friday 30 June 2023	
9:00 - 9:30	**Maria Amparo Ferreira Faustino** *"Insight into porphyrins for antimicrobial environmental applications"*
9:30 - 9:50	**Antonino Mazzaglia** *"Curcumin-loaded Hydrogel generating Photo-antimicrobial Surfaces for the treatment of Periprosthetic Joint Infections"*
9:50 - 10:10	**Francesco Garzella** *"Smart UVC light barriers for the suppression of Airborne Viral and Bacterial Epidemic Spread"*
10:10: 10:30	**Marzia Gariboldi** *"Arene-Ruthenium(II) curcuminoid complexes as photosensitizer agents for antineoplastic and antimicrobial photodynamic therapy: in vitro and in vivo insights"*
10:30 - 10:50	**Nadia Barbero** *"NIR Cyanine dyes for antimicrobial photodynamic therapy"*
10:50 - 11:30	**COFFEE BREAK**
11:30 - 11:50	**Matilde Tubertini** *"BODIPYs-carrier Poly-Methyl-Methacrylate Nanoparticles for Photodynamic Therapy"*
11:50 - 12:10	**Matteo Di Giosia** *"Oligothiophene-albumin bioconjugates as phototheranostic platforms for cancer treatment"*
12:10 - 12:30	**Manuele Di Sante** *"Synthesis of a Chlorin e6 - Fullerene dyad for photodynamic therapy"*
12:30 - 12:50	**Giacomo Insero** *"A pathway towards a persistent luminescent aerosol for antimicrobial-PDI in lung infections"*
12:50 - 13:00	**CLOSING CERIMONY**

Book of abstracts

Invited speakers

Sabrina Conoci

Ultrasensitive PCR-Free Biosensors Based on Photonics Transduction

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The molecular analysis of Nucleic Acids (NA), DNA and RNA, has become nowadays crucial in many medical fields for early and accurate diagnosis, personalized therapy and preventive screening. It is particularly relevant in the field of the infectious diseases as demonstrated by the SARS-CoV-2 virus outbreak. In this scenario, the conventional approach for the molecular analysis of SARS-CoV-2 is based on the PCR (Polymerase Chain Reaction) reaction that, although standardized and consolidated, is quite complex and includes multiple laboratory procedures and high cost that limit, de facto, it massive use. These limitations make the PCR-based analysis inconsistent with the idea of an efficient patient management, in terms of fast diagnosis and prompt answer to the treatment, and viral outbreaks containment. PCR-free approaches allow a fast, ultrasensitive, low-cost identification and quantification of the pathogen with easy-to-use instrumentations representing innovative methodologies suitable for the decentralised and massive infections diagnoses and prevention [1,2,3].

In this contribution PCR- and label-free innovative approaches using photonics transduction are presented and discussed. These approaches were based on the the capturing of whole genomes of pathogens at inorganic surface (silicon or electrode surface) followed by transduction with two photonic methods involving electro-chemical luminescence (ECL) signals and silicon nanowires (Si-NWs) materials.

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Jenny Zhang

Stealing electrons from photosynthesis

Jenny Zhang

Department of Chemistry, University of Cambridge, UK

The 'light reaction' in photosynthesis generates high energy carriers for the 'dark reaction' to carry out carbon dioxide fixation. The biohybrid research community can now electrochemically couple to the photosynthetic electron transport chain (PETC), both in vitro and in vivo, to either extract or insert electrons at various places for fundamental studies and for biotechnological applications.1

In this talk, I will show my group's efforts to steal electrons from cyanobacterial PETC with greater efficiency and control using non-biological approaches. In particular, we utilise tailored 3D-electrodes to enhance the intrinsic activity of the cyanobacteria and to maximise electron exchange.2 We also employ conductive extracellular matrices and exogenous molecular electron shuttles to accelerate extracellular electron transfer between the PETC and the electrode.3,4 The ability to steal electrons from the PETC of living organisms in a controlled manner will open up novel ways to probe and exploit their bioenergetics in biotechnologies.

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Mans Broekgaarden

Spatiotemporal controlled drug delivery with light- and radiotherapy-responsive liposomes.

Mans Broekgaarden

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Liposomes have been the most successful type of nanomedicine for cancer patients, playing a leading role in improving the tolerability of chemotherapeutics. However, to treatment outcomes, new approaches to physically trigger drug release in cancer tissues [1] and increase the permeability of the protective cancer stroma are needed [2]. Therefore, we investigate the development of photo- and radiocatalytic liposomes for remote-controlled drug release that are capable of increasing tumor permeability by excessive oxidative damage to the cancer microenvironment.

Light-controlled drug delivery can be achieved by incorporating porphyrin dyes in the lipid bilayer of liposomes [3]. Upon light excitation, the photodynamically-produced reactive oxygen species oxidize cholesterol and unsaturated phospholipids, resulting in lipid packing defects, and the near-complete release of liposomal cargoes. Using a lipid-conjugated form of the clinically approve photosensitizer verteporfin [4], we developed oxidation-responsive liposomes and discovered that distinct phospholipids act in synergy to promote drug release, prevent lysosomal retention (photochemical internalization), and increase tumor permeability (photodynamic priming).

As an alternative approach, radiation controlled liposomal drug delivery would be a substantial improvement over photo-triggered drug release, as X-rays penetrate deeply into tissues and radiotherapy is broadly involved in the standard-of-care for cancer patients. To achieve this, we adapted our oxidation-responsive liposome formulation, and introduced radiocatalytic gold nanoclusters into the lipid bilayer. Our findings show that a radiocontrolled drug release efficiency of 30% is possible with poly- and monochromatic X-ray sources. We currently investigate the biological effects of these novel radiotherapy-responsive liposomes on pancreatic cancer organoids and in vivo models.

These innovative light- and radiotherapy-controlled liposomes enable spatiotemporal-controlled chemotherapy delivery, with additional improvement in drug efficacy stemming from improved cancer permeability and susceptibility. Such drug delivery systems hold potential to significantly advance the standard-of-care for many cancer patients.

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Valérie Heitz

Targeting the Near-Infrared: π-Extended Conjugates for Photodynamic Therapy and Theranostic Applications.

Valérie Heitz

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Photodynamic therapy (PDT) has several benefits over chemotherapy and radiotherapy in the treatment of localised tumors, including high selectivity, low side effects and immunostimulatory effects.[1] There is also a renewed interest in using PDT to treat infections due to the fast spread of multi-drug resistant bacteria that pose a threat to public health.[2] A major strength of PDT is the absence of bacterial resistance to the treatment and its effectiveness on resistant strains.

Our group has developed photosensitizers for PDT, antimicrobial PDT and theranostic applications which can be excited in the optical therapeutic window for deeper treatment with less photodamage.[3] They are based on porphyrins with an extended π-conjugated system that enable their one or two-photon excitation in the near-infrared (Fig. 1). For antimicrobial PDT, a photosensitizer-antimicrobial peptide conjugate has recently been designed to target and kill bacteria by near-infrared excitation.[4]

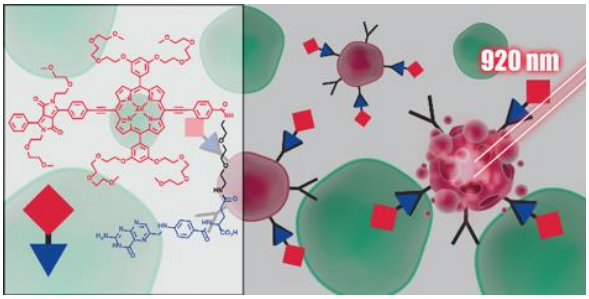

Figure 1. A targeting photosensitizer for PDT in the near infrared.

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Maria Amparo F. Faustino

Insight into porphyrins for antimicrobial environmental applications

Kelly A. D. F. Castro[1], Cátia Vieira[2], Maria Bartolomeu[2,3], Nuno M. M. Moura[1], A. Teresa P. Gomes[2,3], Carlos J. P. Monteiro[1], M. Amparo F. Faustino[1]

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Porphyrin derivatives have garnered significant attention as photosensitizers in photodynamic therapy (PDT) and, more recently, in antimicrobial applications [1,2]. These versatile compounds possess inherent photoactive properties that can be harnessed to address microbial contamination in diferent environmental contexts. Their capacity to generate high levels of reactive oxygen species (ROS) contributes to their potent antimicrobial activity. Porphyrin derivatives, whether in their free form or immobilized on various supports, demonstrated their ability to effectively target and eliminate a wide range of microorganisms, including bacteria, viruses, and fungi, in different environmental conditions [1-3]. Nowadays, applications of porphyrin-based photodynamic antimicrobial treatment (aPDT) extend to areas such as water and wastewater treatment, as well as surface disinfection, among other environmental applications [4-6]. In this communication, the recent advances in the use of porphyrin derivatives as photosensitizer agents for environmental applications will be discussed.

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Young Investigator Award

Gabriella Buscemi

Bio-Inspired Redox-Adhesive Polydopamine Matrix for Intact Bacteria Biohybrid Photoanodes.

Gabriella Buscemi[1,2], Danilo Vona[1], Paolo Stufano[3], Rossella Labarile[1,2], Pinalysa Cosma[1,2], Angela Agostiano[1,2], Massimo Trotta[2], Gianluca M. Farinola[1], and Matteo Grattieri[1,2]

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Anoxygenic phototrophic purple bacteria are well-known microorganisms having a versatile metabolism that allowed using sunlight to oxidize various organic compounds. With the intent to mimic their natural processes, many attempts were made to exploit the ability of energy storage and energy conversion into chemical or electrical energy using biohybrid electrochemical systems. Such approaches allow developing an eco-friendly and scalable technology based on self-repairing biocatalysts where sunlight is utilized as primary green energy source [1]. In the application of living organisms in bioelectronic devices, the challenging aspect is related to the electrochemical interface between biotic and abiotic domains.

In this context, we combined a versatile polymer, polydopamine (PDA), with the purple bacteria *Rhodobacter capsulatus* as biocatalyst. Polydopamine, containing both catechol and amine groups, is a biocompatible polymer suitable for confinement and protection of biomacromolecules [2]. PDA can be obtained by oxygenic self-assembly polymerization of dopamine in water or by electro-polymerization. Moreover, the tunable conductive properties and the key feature of being adhesive onto a variety of surfaces make this material suitable for bioelectrochemical devices.

Herein, we report a one-pot biocompatible and sustainable approach, that provides bacterial cells adhesion under wet conditions to obtain biohybrid photoanodes with facilitated photoinduced electron harvesting [3]. The biopolymer preparation strategy allows it to multiple functions, such as cell protection, adhesion on the surface, and assist electron transfer to the electrode in a stable and durable manner. By immobilizing photosynthetic cells into PDA during its polymerization, while entrapping a quinone-based redox mediator, the biophotoanodes increase up to a 5-fold increase in extracellular electron transfer at the light-dependent biotic/abiotic interface, while maintaining cell viability.

In addition, the sustainability of the approach carries the significant advantage of its *in situ* preparation, paving the way for the future implementation of biohybrid electrochemical systems for sun-powered electrosynthesis of valuable chemicals, as well as biosensing and bioremediation of pollutants in water environments.

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Giorgia Chinigò

Polymethine dyes-loaded solid lipid nanoparticles (SLN) as promising photosensitizers for biomedical applications.

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Polymethine dyes (PMD) have proved to be excellent candidates in the biomedical field for potential applications in both diagnostic and therapeutic. However, PMD application in biomedicine is hindered by their poor solubility and stability in physiological conditions. Therefore, the incorporation of these dyes in nanosystems could be important to prevent the formation of dye aggregates in aqueous environment and to protect their photophysical characteristics. In the present work, two PMD based on the benzoindolenine ring (bromine benzo-cyanine-C4 and bromine benzo-squaraine-C4) were incorporated into Solid Lipid Nanoparticles (SLN) to solubilize and stabilize them in aqueous solutions. Obtained SLN showed a high incorporation efficiency for both PMD (~ 90%) and not only preserved their spectroscopic properties in the NIR region even under physiological conditions but also improved them. Viability assays showed good biocompatibility of both empty and loaded nanocarriers while the cellular uptake and intracellular localization showed the effective internalization in MCF-7 cells, with a partial mitochondrial localization for CY-SLN. Moreover, in vitro phototoxicity assay showed that cyanine loaded-SLN (CY-SLN) is more photoactive than the free dye [1].

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Oral Communications

Nadia Barbero

NIR Cyanine dyes for antimicrobial photodynamic therapy.

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Antimicrobial photodynamic therapy (aPDT) has emerged as a promising strategy to improve antimicrobial treatments and face the antibiotic resistance of conventional therapies. Among the different photosensitizers, Near Infrared (NIR) polymethine dyes (Squaraines, SQs and Cyanines, CYs) have attracted considerable attention although their poor aqueous solubility and stability still limit their application [1]. Their incorporation inside nanoparticles (NPs) or into electrospun fibers could help to prevent dye aggregation, protect their photochemical properties, and play a key role in the infection treatment.

In the present work, three Cys were synthesized and characterized [2]. Their ability to produce Reactive Oxygen Species (ROS), responsible of bacterial death, was evaluated, and compared with Toluidine Blue as reference. Furthermore, *in vitro* antimicrobial studies against Gram-positive models showed a good antimicrobial effect after irradiation, confirming the potential of some of these organic photosensitizers for aPDT in the local treatment of infections.

The most promising dye has been then integrated in a polymeric based electrospun dressing [3] in order to locally activate the released NIR dye to remove pathogenic bacteria after irradiation. Among the others, Br-CY showed an interesting *in vitro* antimicrobial activity compared to the standard vs Gram negative bacteria, suggesting that NIR- polymethine dyes may be considered valuable photosensitizers for aPDT. However, additional experiments are ongoing to evaluate the antimicrobial behaviour of the dye-loaded electrospun fibers, to be used in the treatment of localized infections.

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Acknowledgments

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Matteo Calvaresi

NanoPhages: Photoactive bacteriophages for receptor targeted PDT

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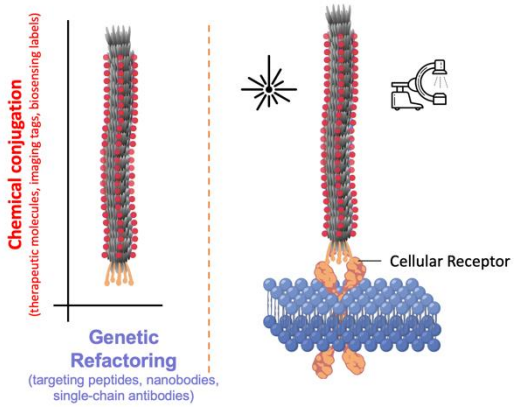
An orthogonal nanoarchitectonics approach (genetic/chemical) was developed to engineer M13 bacteriophages as phototheranostic platforms able to simultaneously detect, image and kill cancer cells, upon light irradiation [1,2]. M13 was genetically refactored to display on the phage tip a peptide, [1,2] a nanobody or a single chain antibody able to bind epidermal growth factor receptors such as EGFR or HER2. Using an orthogonal approach to the genetic display, the refactored phages were then chemically modified, conjugating hundreds of photosensitizers on the capsid surface [1,2] or transforming the viral capsid in a oligothiophene "living" nanoparticle.



Flow cytometry and confocal microscopy experiments demonstrated the efficient retargeting of the phages to cancer cells overexpressing EGFR/HER2. The killing activity of cancer cells was observed at picomolar concentrations of the phage vector. The phage-bioconjugates showed a high permeation/PDT activity also into 3D spheroids.

The nanosafety of the phototheranostic platform and its imaging/PDT performancences were evaluated *in vivo* using *Hydra vulgaris* as a model organism.

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Paolo Emidio Costantini

A modular phage vector platform for targeted photodynamic therapy of Gram-negative bacterial pathogens.

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Growing antibiotic resistance has encouraged the revival of phage-inspired antimicrobial approaches. On the other hand, photodynamic therapy (PDT) is considered a very promising research domain for the protection against infectious diseases. Yet, very few efforts have been made to combine the advantages of both approaches in a modular, retargetable platform. Here we foster the M13 bacteriophage as a multifunctional scaffold enabling the selective photodynamic killing of bacterial cells. We took advantage of the well-defined molecular biology of M13 to functionalize its capsid with hundreds of photo-activable Rose Bengal sensitizers and contemporarily target this light-triggerable nanobot to specific bacterial species by phage-display of peptide targeting moieties fused to the minor coat protein pIII of the phage. Upon light irradiation of the specimen, the targeted killing of diverse Gram (-) pathogens occurred at subnanomolar concentrations of the phage vector. Our findings contribute to the development of novel antimicrobials based on targeted and triggerable phage-based nanobiotherapeutics.

Maria Alexandra Cucu

Photoinactivation of *Pseudomonas aeruginosa* and *Staphylococcus aureus* biofilm by a non-uniform LED illumination method

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Photodynamic inactivation of multidrug-resistant pathogens responsible for chronic lung infections is at the forefront of phototherapy applications to internal organ diseases. To meet the challenging demand of a non-invasive illumination of all the relevant airways up to alveoli, a novel aerosolized phosphorescent-particle-based light source has been recently proposed [1]. The principal aim of this study was to measure the photosensitivity of *Pseudomonas aeruginosa* and *Staphylococcus aureus* strains, e. g. *PAO1 - reference* and *LESB65 - clinical* and *USA300 - reference* and *CF-MRSA - clinical* respectively, in the absence of external photosensitizers and at different irradiation wavelengths. Bacterial biofilms were grown (4 days for *P. aeruginosa* strains and 7 days for *S. aureus* strains) on Nunc-TSP lid systems and photo-inactivated by 4 different setups based on LED sources peaked at 415, 445, 525 and 623 nm respectively. A 2D non-uniform illumination protocol was employed to deliver different doses (10 to 110 J/cm^2) in a single experimental run. Post-irradiation CFU counting respect to non-irradiated controls was performed and compared with the predictions of a previously defined semi-theoretical model [2]. The biofilm photoinactivation was studied as a function of both dose and illumination wavelength. Irradiation at 415 nm resulted in the best dose-dependent antimicrobial activity for all the tested strains. A reduction of at least 2 log CFU/peg at 60 J/cm^2 was observed for PAO1, LESB65 and CF-MRSA strains, while in the case of USA300 strain a reduction of 1 log CFU/peg has been observed, reaching 1.5 log CFU/peg at the maximum irradiation dose (110 J/cm^2). Also 445 nm light resulted in a dose-dependent antimicrobial activity, but with about 1 log CFU/peg reduction at 60 J/cm^2 for all strains. Scant effect or no effect was observed at both 525 and 623nm at any dose for all the tested strains, except for LESB65 irradiated at 525 nm, showing a reduction of about 1 log CFU/peg at 60 J/cm^2.

These results may offer important indications for aerosolized light source synthesis and definition of its most effective emission spectrum to achieve the most effective therapeutic treatment.

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Matteo Di Giosia

Oligothiophene-albumin bioconjugates as phototheranostic platforms for cancer treatment.

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The electronic, optical, and redox properties of thiophene-based materials have made them pivotal in nanoscience and nanotechnology. However, the exploitation of oligothiophenes in photodynamic therapy is hindered by their hydrophobicity which lowers their biocompatibility and availability in physiological environments. The conjugation of oligothiophenes molecules to protein carriers can overcome this limitation [1].

Here we designed, synthesized, and characterized four thiophene-based oligomers (Figure 1), consisting of three thiophene rings (donor groups, D) and one benzothiadiazole (acceptor group, A). The position of the acceptor group in the molecular structure produces different combinations of acceptor and donor groups, allowing the tuning photophysical properties of the oligothiophenes. A terminal N-hydroxysuccinimidyl (NHS) ester was inserted into the oligothiophene scaffold for bioconjugation with protein amines.

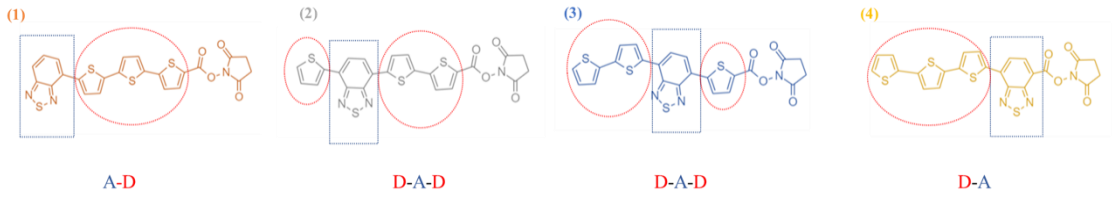

Figure 1. Molecular structures of the oligothiophene-NHS

The bioconjugation of the synthesized oligothiophenes with human serum albumin (HSA) affords the exploitation of insoluble oligothiophenes as photosensitizers in physiological environments. All the bioconjugates are water-soluble, biocompatible, and preserve HSA in monomeric form. While they do not show any dark toxicity, upon irradiation with low light doses, the bioconjugates efficiently produce reactive oxygen species (ROS) and lead to the complete eradication of cancer cells, in the nanomolar range of HSA concentration.

The HSA-oligothiophene bioconjugates are novel phototheranostic platforms able to generate ROS intracellularly and, at the same time, provide imaging possibilities, exploiting the intrinsic fluorescence of the oligothiophene.

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Manuele Di Sante

Synthesis of a Chlorin e6 - Fullerene dyad for photodynamic therapy.

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Chlorin e6 (Ce6) is one of the most widely used photosensitizers, due to its high efficacy in singlet oxygen generation, low dark toxicity and great absorption in the red region of the visible spectrum (650-700 nm).[1] However, due to the negative charges of the carboxylic groups of Ce6, its performances as photosensitizer are hampered by a limited ability to permeate the cellular membrane.

Fullerenes are nanomolecular carbon cages that can serve as platforms for the delivery of drugs and imaging agents, because of their ability to pass through cell membranes to deliver therapeutic molecules.[2] Here we synthesized and fully characterized a covalent Chlorin e6 - Fullerene dyad (C_{60}-Ce6) (figure 1).

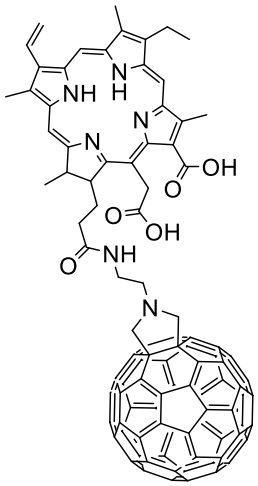

Figure 1. Chemical structure of the Chlorin e6 – Fullerene dyad synthesized

In vitro tests demonstrated, as expected, the enhancement of the cellular uptake of the C_{60}-Ce6 molecule compared to free Ce6, along with an increased killing efficacy of the dyad, upon irradiation with red light.

The ROS production of the dyad was also investigated. Upon irradiation with red light, C_{60}-Ce6 showed a large production of ROS via both type I (peroxides) and type II (singlet oxygen) mechanisms. In particular, the type I pathway was largely enhanced compared with free Ce6, suggesting the formation of an interacting antenna-fullerene system.[3]

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Mariachiara Gani

Can photodynamic therapy treatment overcome drug resistance in pancreatic cancer cells?

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Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal human diseases, with a 5-year survival rate of less than 10%. Treatment of PDAC is notoriously difficult, as it easily develops resistance to current therapeutic agents after chronic treatments. One of the standard adjuvant anticancer therapy is based on gemcitabine (GEM), a chemotherapeutic agent that can halt cancer cell growth by inhibiting DNA synthesis. Like most chemotherapeutic agents (e.g., cisplatin, paclitaxel, doxorubicin, etc.), GEM also acts by increasing reactive oxygen and nitrogen species (ROS/RNS).

It is reported that the development of resistance may depend on the levels of ROS and nitric oxide (NO)/RNS, which play both cytotoxic and cytoprotective roles [1,2]. We confirmed this in our previous work on photodynamic therapy (PDT): PDT can increase the production of ROS and NO through the induction of NO synthase (iNOS), and we have seen that chronic treatment with suboptimal PDT dose (i.e., constant oxidative stress) can promote a more aggressive and resistant population, while an acute treatment with high doses leads to cancer cell death. Indeed, low ROS and RNS levels have a cytoprotective role by targeting signaling pathways involved in the upregulation of cell survival and proliferation/growth [3].

We developed a PDAC cell line BxPC-3 resistant to GEM (BxPC-3/GEM Res) by repeatedly treating BxPC-3 cells with low doses of GEM (30 nM) for months. It was found that a dose range treatment with GEM is able to increase the levels of ROS and NO in both parental and resistant cells, while keeping them lower in the BxPC-3/GEM Res line compared to the parental cells.

Thus, the aim of this work is to demonstrate if PDT treatment is able to modulate the levels of ROS and NO/RNS in the BxPC-3/GEM Res cell line, leading to cell death and the arrest of drug resistant cancer cells proliferation.

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Marzia B. Gariboldi

Arene-Ruthenium(II) curcuminoid complexes as photosensitizer agents for antineoplastic and antimicrobial photodynamic therapy: in vitro and in vivo insights.

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In the last decades, photodynamic therapy (PDT) has gained considerable attention as a new modality of treatment for cancer and as an antibacterial strategy. PDT uses compounds known as photosensitizers (PSs) that, after being excited by light at specific wavelengths and reacting with molecular oxygen, generate reactive oxygen species and induce cell death. PDT presents greater selectivity towards tumor cells than conventional chemotherapy; however, PSs have limitations which have prompt the research of new, more favourable PSs. In this context, the development of new naturally derived compounds to be used for anticancer or antibacterial PDT led to the observation that curcumin and also different curcuminoids are capable to significantly inhibit cell viability in both cancer cell lines and bacterial strain. Nevertheless, its low water solubility, rapid metabolism, interference with other drugs, and low stability limit the use of curcumin as a PSs. Therfore, chemical modifications have been proposed to enhance the activity of curcumin. In particular, metal-based-PSs, expecially those complexed with ruthenium(II), have attracted considerable attention.

The aim of this study was the chemical and biological characterization of some arene-ruthenium(II) curcuminoids for anticancer and antibacterial PDT. First, hydrophilicity, photodegradation rates and singlet oxygen production capacity of the candidate compounds were evaluated. Subsequently, the photodynamic effects on human colorectal cancer cell lines were assessed, along with the ability to induce the increase of ROS levels and apoptotic, necrotic and autophagic cell death. In addition, the possible toxic effects of the arene-ruthenium(II) curcuminoids were investigated using the larvae of *Galleria mellonella* (Lepidoptera, Pyralidae, Gm) as *in vivo* model. Finally, the antimicrobial activity of the compounds was evaluated on Gram-negative and Gram-positive models.

Regarding the results on tumor cell lines, similar or better photodynamic effects were observed for arene-ruthenium(II) derivatives, compared to their curcuminoid precursors. An interesting, albeit low, antibacterial activity on Gram positive B. subtilis strain was also observed. Interestingly, arene-ruthenium(II) derivatives did not show significant *in vivo* toxicity on *Galleria mellonella*.

Overall, the results obtained indicate that the arene-ruthenium(II) derivatives deserve further studies and that these compounds could be represent a novel class of PSs for cancer PDT.

Francesco Garzella

Smart UVC light barriers for the suppression of Airborne Viral and Bacterial Epidemic Spread

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After the global spread of SARS-CoV-2 pandemic the role of airborne transmission of pathogens became of high interest. Nowadays it is known that airborne infections, including COVID-19, are conveyed by micrometric particles, referred as droplets, ejected by coughing and sneezing [1] which, depending on their size, may precipitate or persist in the air, transmitting the infections. Despite the new prevention strategies based on vaccines and face masks or antibiotics for viral and bacterial infections several issues including the mutations for viruses and the antibiotic resistance for bacteria neutralize these approaches. From literature it is evident that since absorption maxima of DNA and RNA lay in the range 200–280 nm [2, 3], the UVC light might be the most effective to induce damages and inactivate viruses and bacteria. However, many UVC commercial systems are based on Mercury lamps having an emission at 254 nm that is harmful for human skin. The development of new excimer lamps in the UVC range is focusing research on wavelengths around 220 nm that penetrate few µm into the superficial *stratum corneum* of the skin; this prevents light absorption by the underlying live tissue [3, 4] and makes these sources safer for the application in humans and effective to induce RNA/DNA damages.

In this work we propose an innovative light barrier combining a 222 nm illumination system with a vertical flux of air that conveys exhaled particles to the light source and controls humidity and temperature, crucial parameters for virus diffusion, for the suppression of airborne viral and bacterial spread to be used in situations with constrained geometries (e.g., public transportation, offices, waiting rooms etc.) in presence of humans. After UVC-induced ozone production test and light emission characterization of a 222 nm excimer KrCl mixture lamp (USHIO Care222Ò), we performed *in-vitro* photo-sterilization of both SARS-CoV-2 cultures (Wuhan lineage) and two bacterial strains of *Pseudomonas Aeruginosa* and *Staphylococcus Aureus* (reference wild-type and clinically relevant), that are the most isolated pathogen from the airways of *cystic fibrosis* patients harboring relevant antibiotic resistance infections. We demonstrate a strong photo-killing efficacy of 4-log reductions for SARS-CoV-2 (Spearman-Kraber method) and 3-log reduction for all the bacterial strains (viable cell counts method) after irradiation with 222 nm up to 35 mJ/cm^2 fluence range. Alongside, starting from the evidence of COMSOL MultiphysicsÒ simulations, we designed an *in-vitro* system to demonstrate the sterilization efficacy of 222 nm light on epidemic spread mimics is in progress as an *in-vivo* experiment with mice will as a last step to fully demonstrate the capabilities of this innovative UVC light barrier.

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Giulia Giugliano

Identification by virtual screening of fullerene carrier proteins for PDT applications

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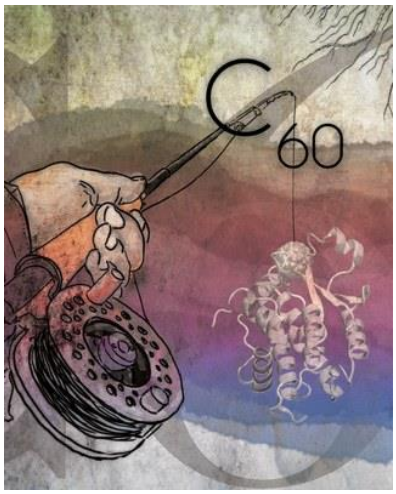

Fullerenes are considered ideal photosensitizers[1] because they are characterized by: I) an high quantum yield (nearly 100%); II) the ability to generate ROS with both the type I (electron transfer) and type II (energy transfer) mechanisms; III) resistance to photobleaching, IV) the possibility to functionalize their cage with light-harvesting antennae to change the wavelengths of absorption towards the red/NIR region of the spectrum.

However, the insolubility of fullerenes in a physiological environment and the formation of aggregates, hamper their full exploitation. Fullerene monodispersity is a crucial feature for their potential application in PDT. We already demonstrated that proteins behave as supramolecular hosts to disperse C_{60}[2,3] and C_{70}[4] in water, preserving their chemical and photophysical properties.

This project aimed to find new proteins that can be used as dispersing agents for C_{60} among the *AlphaFold Human Proteome* database (23.391 proteins). A reverse docking protocol was used to obtain a ranking of the most interacting proteins with C_{60}.

Proteins with a β-propeller structure, belonging to the solenoid class, were identified as ideal supramolecular hosts of C_{60}: these proteins are characterized by a "donut"-shaped domain (WD, Kelch, and RCC domains) where C_{60} fits perfectly. Natural carrier/transport proteins were also identified as potential C_{60} delivery systems.

A statistical analysis of the most interacting amino acids with C_{60} allows the identification of the residues responsible for the interaction of a protein with the fullerene. The driving force for the fullerene binding is represented by the formation of π-π interactions with aromatic amino acids (Phe, Tyr, Trp) and hydrophobic interactions with aliphatic (Leu, Ile, Met) side chains.

Giacomo Insero

A pathway towards a persistent luminescent aerosol for antimicrobial-PDI in lung infections

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Antimicrobial photodynamic inactivation (aPDI) has the potential to play a major role in addressing the global issue of multidrug resistance. However, it faces a significant drawback in the availability of a suitable illumination system, particularly when the target is not easily accessible with external light sources. Currently, deep tissue illumination is performed invasively, such as through interstitial optical diffusive fibers or during surgical operations [1]. Therefore, the search for a non-invasive illumination system is of utmost importance and presents a considerable challenge.

To overcome the light penetration problem in patients with antimicrobial-resistant lung infections, such as those affected by cystic fibrosis, we have developed an aerosol based on persistent luminescence particles [2]. This aerosol acts as a non-invasive and inhalable light source. 300-nm spherical particles consisting of ZrO_2 material doped with Ti^{4+} are functionalized through a PEGylation reaction to achieve high stability in a water suspension. These particles exhibit maximum absorption at 280 nm and emit a broad blue-light spectrum centered around 470 nm, with a full-width at half maximum of approximately 100 nm. The particle photoluminescence, induced by continuous excitation at 280 nm, has been characterized at different timescales, ranging up to a few seconds. The long persistence luminescence observed in the second timescale accounts for a small percentage of the overall luminescence. The particle emission efficiency was calculated to be around 8% through calibrated quantum yield measurement conducted using an integrating-sphere fiber-coupled to a spectrometer.

In order to assess the efficacy of aPDI, we defined preliminary *in vitro* photo-killing experiments using ZrO_2:Ti^{4+} particles as a light source to target the bacterial growth of the *Pseudomonas aeruginosa* clinical strain (LESB65 [3]). *P. aeruginosa* is a significant pathogen involved in chronic lung infections and exhibits relevant antibiotic resistance mechanisms. Bacterial suspensions (at 0.5 McFarland optical density) were spotted on nitrocellulose membranes and irradiated for 24 hours with particle luminescence to deliver a total light dose of 20 J/cm^2. The inhibitory activity of particle luminescence was evaluated by viable cell count. The chosen light dose value was based on previous experiments where a 415-nm light-emitting diode (LED) was used to illuminate the biofilm and demonstrate its inhibitory activity. In the first experiments, the ZrO_2:Ti^{4+} particle luminescence did not significantly affect the biofilm growth of *P. aeruginosa*, while the LED illumination did. We are currently exploring various photokilling enhancers to achieve significant photokilling when utilizing light emitted by the particles.

This innovative approach of delivering light to the lungs using a phosphorescent-based aerosol could become an efficient tool in combating antimicrobial resistance in lung infections in the future.

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Rossella Labarile

Coffee-based photoelectrochemical system with Rhodobacter sphaeroides

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Photosynthetic purple non sulfur bacteria are anoxygenic microorganisms with versatile metabolism, as they use sunlight to oxidize a broad variety of organic compounds in addition to heterotrophic and photoautotrophic alternative metabolisms [1]. The use of photosynthetic bacteria for the sustainable valorization of the huge amount of waste produced by agricultural systems represents an eco-friendly, cost-effective, and socially acceptable agri-waste management technology [2]. *Rhodobacter* (*R.*) *sphaeroides* was selected for its ability to rapidly adapt to several growth media [3].

Coffee is one of the most consumed beverages in the world and its consumption is associated with huge amounts of waste and spent coffee grounds [4]. Based on the promising evidence of their photo-metabolism on coffee and coffee-waste based media, we explored the possibility of developing bio-hybrid photoelectrochemical systems. We showed that *R. sphaeroides* is able to generate a measurable photocurrent at bio-hybrid interfaces by using green coffee extracts, and more specifically chlorogenic acids, as effective mediators for Extracelluar Electron Transfer (EET). Moreover, the preliminary results obtained by coupling such system with bio-based carbon composite electrodes recently developed [5], pose the foundation for a new class of circular and coffee-based bio-hybrid photoelectrochemical systems.

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Maya Dimova Lambreva

Photosystem II electron transport rerouted by single-walled carbon nanotubes.

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The development of various biohybrid natural or artificial systems to enhance solar energy conversion is a high priority in contemporary energy research. The fusion of highly dynamic and adaptive photosynthetic structures with easily manipulated inorganic materials at nanoscale could open new opportunities for the development of solar-powered biotechnology for renewable energy production. In this context, the distinct photochemical and electrochemical properties of single-walled carbon nanotubes (CNTs) have stimulated research interest in nanomaterial utilization in various *in vivo* and *in vitro* photosynthetic biohybrid setups. The mechanism of interaction between the nanotubes and photosynthetic structures is still unclear. The limited number of studies on the interplay between CNTs and photosynthetic complexes provides controversial indications of the energy flow within the biohybrid system. Our studies on *in vivo* effects of nanotubes on photochemical reactions of green alga *Chlamydomonas reinhardtii* indicate that the CNTs can alter the electron transport of Photosystem II and may facilitate the non-radiative loss of excitation energy [1]. To gain further insight into these processes, we analyzed the electro-optical interactions of CNTs with isolated photosynthetic structures of varying complexity. Analyzing the possible pathways of energy decay in the model systems studied, our results indicate a possible leakage of photosynthetic electrons towards the nanotubes, most likely at the level of the Photosystem II acceptor site [2].

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Sofia Leo

The radiotherapeutic effects of photosensitizers: An overview of the physical, chemical, and biological mechanisms

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Significance: Radiotherapy is widely implemented for the treatment of the head and neck, breast, cervix, prostate, eye, thyroid and also gastroenteropancreatic and neuroendocrine tumors [1]. New technologies have paved the way to safer radiotherapy regimens, such as brachytherapy, stereotactic- and intensity-modulated radiotherapy, but the efficacy still requires improvements. Inorganic nanoparticles are frequently explored as radiosensitizing agents [2][3], but studies have also emerged that report on the radiosensitizing properties of porphyrins and other photosensitizers [4]. As these events remain poorly understood, the aim of our research is to shed light the interaction between these photosensitizers and ionizing radiation.

Approach: We systematically summarized the findings of 54 studies in which radiosensitization by photosensitizers was reported.

Results: Out of 54 papers on radiosensitization with photosensitizers, 18 papers reported on ALA or PpIX, 6 papers on verteporfin, 7 papers on photofrin and 23 papers on other photosensitizers. The studies have demonstrated that in presence of photosensitizers, radiotherapy causes elevated ROS production in physicochemical experiments [5], and increased cell death and tumor growth inhibition in biological experiments. This was observed in a broad dose-range for diverse types of radiation (e.g., X-ray dose-range $100\mathrm{eV}$-$100\mathrm{keV}$). To understand how this happens, we reviewed the fundamental mechanisms of radiotherapy. Photosensitizers are typically excited with visible photons of >1.5 eV, and electrons and photons with similar energies are generated via the Auger effect, pair production, Bremsstrahlung effect and Cherenkov radiation. These effects may thus be responsible for the excitation of porphyrins and other photosensitizers, yet controlled experiments to identify the dominating effects are missing. In biological studies, several photosensitizers were shown to interfere with cell signaling events, which was shown to increase the susceptibility of the cells to radiotherapy.

Conclusions: The interactions between secondary electrons and photons during radiotherapy can catalyze the production of toxic reactive species and increase treatment efficiency. Porphyrins and other photosensitizers are therefore promising radiosensitizing agents.

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Miryam Chiara Malacarne

Evaluation of nanoparticles covalently bound with a BODIPY for their possible PDT applicability.

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The advance of early tumors diagnosis and the growing interest in conservation of normal tissue during cancer surgery has led to the growing demand for minimally or non-invasive therapeutic methods, such as photodynamic therapy (PDT) [1]. PDT is based on the activation of a photosensitizer (PS), with light at an appropriate wavelength and in the presence of oxygen, to produce reactive oxygen species (ROS) responsible for cellular damages leading to cell death [2]. However, this therapeutic modality has some limitations, such as the poor water solubility of PSs and their limited selectivity. To overcome these problems, in recent years research has exploited nanoparticles (NPs) that can enhance the solubility of PSs as well as the selectivity of treatment by promoting tumor targeting and intracellular delivery of the PS payload [3].

The aim of this project was to synthesize a PS, belonging to BODIPY family [4], covalently bind to NPs which differ from each other in their lipophilic character, and then evaluate the photodynamic activity of PS both in free form and in NPs. *In vitro* tests were performed on SKOV3 and MFC-7 tumor cell lines. To better explain the mechanism of the photodynamic process, further analyzes were performed using flow cytometry (uptake, apoptosis, and necrosis).

Chemical-physical analyzes demonstrated that both NPs are suitable for PDT as they are resistant to photobleaching and have a good singlet oxygen ($^1O_2$) production.

In vitro biological analyzes showed how BODIPY in free form has a higher photodynamic activity than the NPs bounded counterpart; this data was also confirmed by the greater free BODIPY absorption by cells.

To better understand the main mechanism of PDT-induced cell death mechanisms, cytofluorimetric analyzes showed how free BODIPY addresses necrotic process while NPs prefer apoptosis.

The scratch wound healing assay verified how all the compounds are able to partially inhibit cell migration, intrinsic in SKOV3 cells.

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Giacomo Mandriota

Winogradsky column as tool for microbial communities enrichment

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Recently, as the awareness of the crucial role of bacteria in the environment and human life has escalated, scientists have employed advanced technologies to emphasize the communal and interconnected aspects of microbial communities. Photosynthetic Purple Non-Sulfur Bacteria (PNSB) as model organisms for studying bacterial photosynthesis are an important example.[1] In this scenario, the Winogradsky column (WIC) is a very promising candidate to investigate the ecology of microbial communities in soils and sediments, using samples of water, mud and nutrients.

The WIC can be used also to research specific bacteria through the enrichment of cultures. Microbial activity and abiotic processes in the columns create chemical and environmental gradients promoting several niches for microbial growth, with light serving as primary energy source for primary producers. The outcome is the formation of a well-organized microbial ecosystem capable of carrying out all essential processes required to sustain the nutrient cycle.[2] WICs can serve as a valuable tool for studying how environmental factors impact microbial community structure and dynamics. Furthermore, WICs can be indeed maintained or manipulated in a laboratory setting allowing careful control.[3]

Herein, we constructed an experimental column by using a glass cylinder that contains a mixture of mud, water, and other nutrients to simulate a real environment. Several sediment and sediment-water samples were collected from different sampling points selected as a model of a microbial ecosystems. Nutrients within the column generate gradients in which different bacteria thrive. The microbial community is kept in balance by the production of oxygen, from algae and/or cyanobacteria colonizing the surface, while photosynthetic bacteria are found further down. To enable the growth of photosynthetic bacteria and the formation of both anaerobic/aerobic and sulfur concentration gradients, the experimental column was positioned adjacent to a window, ensuring direct exposure to light radiation. The preliminary results achieved are encouraging and demonstrate the experimental column as an efficient enrichment-culture approach that can enhance our understanding of the diversity and ecology of different bacteria in soils.

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Marconi Alessia

Human Serum Albumin: an effective drug delivery system for photodynamic therapy

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Dispersion of photosensitizers (PSs) in their monomeric form with plasma proteins, before administration, can confer solubility to hydrophobic PSs and increase their biocompatibility, by hosting the PS through non-covalent interactions.

Human Serum Albumin (HSA) is the most abundant carrier protein in the blood. Due to the enhanced permeability and retention effect (EPR), as well as the presence of HSA receptors overexpressed on cancer cells, HSA displays tumor targeting potentials and it can be used to develop biocompatible protein-based nanoplatforms for cancer theranostics. Here we demonstrated the possibility to exploit HSA as a carrier for hydrophobic PSs such as chlorin e6 (Ce6) and temoporfin (mTHPC).

Ce6@HSA and mTHPC@HSA complexes (Figure 1) - characterized by a well-defined 1:1 stoichiometry -were synthesized and characterized. The specific binding pocket of Ce6 and mTHPC in HSA were identified computationally and the atomistic details of their interactions were provided.

The complexes are stable in a physiological environment, do not aggregate, and are extremely efficient in PDT performance. Due to the stabilizing effect of HSA which, i) avoids the formation of aggregates, ii) reduces the self-quenching of the excited state of PSs, the PS@HSA complexes show enhanced production of ROS when compared to the free PSs. mTHPC@HSA induces cytotoxicity in HNSCC cell lines, upon irradiation, increasing intracellular ROS generation and the number of γ-H2AX foci, a cellular event involved in the global response to cellular stress. These results highlight the important role of HSA as a delivery system for PSs.[1,2]

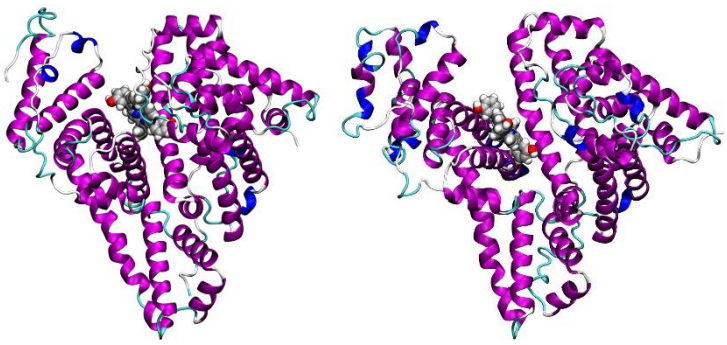

Figure 1. Ce6@HSA (left) and mTHPC@HSA (right) complexes

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Tainah Dorina Marforio

Designing phototheranostic platforms by in silico approach

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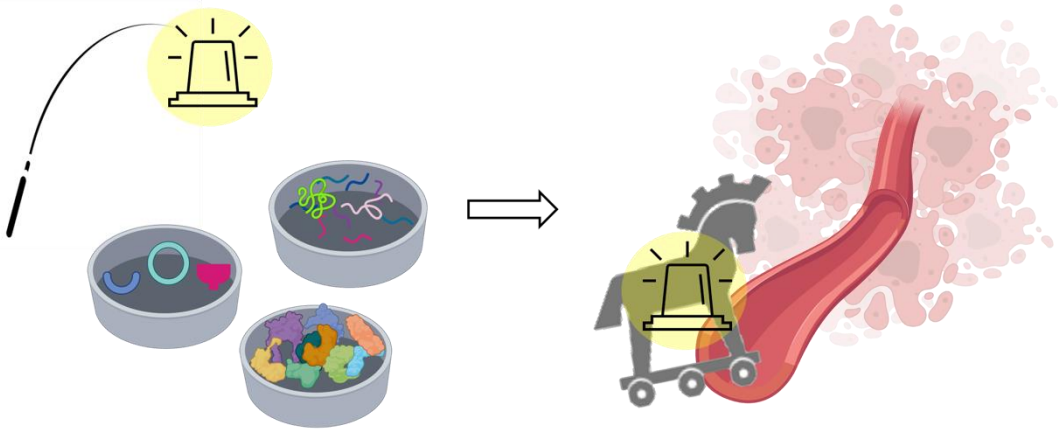
Many photosensitizers (PSs) used in Photodynamic Therapy (PDT) are highly hydrophobic and their lipophililcity hampers their full exploitation. In oder to achieve water solubility, biocompatibily, high reactive oxygen species (ROS) generation and low tendency of aggregation, PSs need to be “hidden” inside carriers. Proteins are ideal candidates to transport and deliver PSs to the biological targets, acting as “Trojan Horses” by (i) hiding the PSs, (ii) controlling their cellular uptake, (iii) driving their crossing of physiological barriers, and (iv) ultimately governing their biological fate.[1] From the experimental point of view, finding the right PS protein-carrier, among thousands, can be challenging, if not impossible. Computatioinal approaches may come in aid: available and downloadable protein databases (AlphaFold, PDTD) or purpose-built databases (Plasma Protein Database, Heme Protein Database) can be exploited as pools where the molecule of interest is the bait, fishing out the most promising proteins able to bind and carry it.[2-5] The present talk will focus on showing the computational protocol developed in our research group (NanoBioInterface Lab@UNIBO), which has already demonstrated to be an indispensable and realiable tool to support the finding of promising protein-carriers for PSs.



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Elisa Martella

Mesenchymal Stromal cells as active carriers of chemo and photodynamic therapy-based nanoparticles for osteosarcoma treatment.

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Osteosarcoma (OS) is the most common type of bone tumor and is characterized by varying degrees of malignancy [1,2]. High-grade OS (HGOS) is the most aggressive subtype with a favorable outcome only in 60-65% of patients who are under 40 years old and with localized and non-metastatic disease at clinical presentation [3]. A promising approach enhancing osteosarcoma prognosis involves the combination of various techniques, such as chemo- and photodynamic therapy, delivered through nanocarriers for synergistic cell death [4,5]. Among the potential candidates for improving drug accumulation at the tumor site, mesenchymal stromal cells exhibit a significant advantage due to their tumor-homing ability and intracellular drug retention. In this study, we evaluated the efficacy of chemo-releasing and photoactive bimodal nanoparticles, kPCe6 NPs, delivered via stromal cells. In vitro analyses show that cells internalize and retain kPCe6 NPs in a dose-dependent manner and that kPCe6-loaded cells induce massive tumor cell death in a tridimensional tumor model. However, results from an in vivo orthotopic osteosarcoma murine model show negligible tumor cell death upon peritumoral administration of 2 doses containing 10^6 loaded cells. To gain insight into this observation, the role of cell dose in treatment efficacy was investigated in tridimensional models. Our results indicate that achieving a tumor reduction higher than 90% requires a substantial number of loaded cells, approximately 35% of the entire tumor mass, highlighting the criticality of the cell dose for the success of this therapeutic approach and its potential impact on clinical translation in osteosarcoma patients, particularly when the number of tumor cells is limited.

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Edoardo Jun Mattioli

Identification of Blood Transport Proteins to Carry Temoporfin: A Domino Approach from Virtual Screening to Synthesis and In Vitro PDT Testing.

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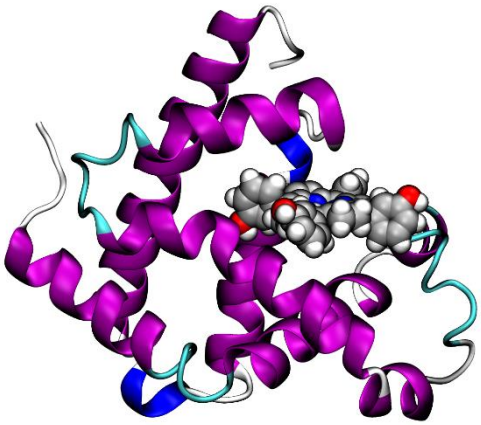

Figure 2. mTHPC@apoMb structure

Temoporfin (mTHPC) is a clinically approved photosensitizer (PS) drug in photodynamic therapy (PDT). The lipophilic nature of mTHPC poses challenges in fully exploiting its therapeutic potential. The poor solubility in physiological environments causes dark toxicity and reduces the generation of reactive oxygen species (ROS).

In this study, we used a reverse docking approach to identify several blood transport proteins able to bind and disperse mTHPC at the molecular level. These proteins include apohemoglobin, apomyoglobin, hemopexin, afamin, and human serum albumin.

Based on computational results, we synthesized the mTHPC-apomyoglobin complex (mTHPC@apoMb, Figure 1) and demonstrated its ability to monodisperse mTHPC in physiological environments. The mTHPC@apoMb complex retains the imaging properties of mTHPC while the capacity to generate ROS through both type I and type II mechanisms are enhanced.

In vitro experiments demonstrated the efficacy of the photodynamic treatment using the mTHPC@apoMb complex. Blood transport proteins can be used as molecular "Trojan horses", overcoming the current limitations of mTHPC by conferring (i) water solubility, (ii) monodispersity, and (iii) biocompatibility. [1,2]

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Antonino Mazzaglia

Curcumin-loaded Hydrogel generating Photo-antimicrobial Surfaces for the treatment of Periprosthetic Joint Infections

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Periprosthetic joint infections (PJI) after the surgery are disastrous complications, leading to a severe health and financial burden for patients. PJI events are mainly caused by *Staphylococcus aureus* and nearly 60% of them are methicillin-resistant *S. aureus* (MRSA) resulting in a high rate of treatment failure. The current antibiotic therapy mainly relies on vancomycin (Van) use, even if various reports showed the emergence of vancomycin-resistant enterococci (VRE). At the same time, Van may also have some considerable side effects, such as ototoxicity and nephrotoxicity, during the antibacterial treatment. To overcome these drawbacks, antimicrobial photodynamic therapy (aPDT) is a good candidate both to prevent and fight the PJI.[1] Within our ongoing research on novel biomaterials based on nanophototherapeutics,[2,3] here we adapted the properties of antimicrobial surface by spreading a resorbable hydrogel based on DAC® (hyaluronic acid conjugated to polylactic acid, HA-PLA) produced by Novagenit[1] (Mezzolombardo, Trento) loaded with curcumin (Curc) capable of increasing water solubility, bioavailability and to control the release of Curc within the infection site. With the aim of helping to overcome antimicrobial-resistance and reduce the antibiotic dosage with minimal side effects, an analogue hydrogel was formulated in the presence of both Curc and Van. The interaction between Curc and DAC® in the hydrogel was studied using complementary spectroscopic techniques such as UV/Vis spectroscopy, fluorescence, Dynamic Light Scattering (DLS), and ζ-potential measurements. The stability and erosion kinetics of the hydrogels were evaluated in biologically relevant media to ensure control over time and efficacy. In addition, titanium surfaces mimicking prostethic scaffolds were coated by hydrogels and on them the photo-antimicrobial activity against MRSA, VRE, and *Pseudomonas aeruginosa* strains was evaluated using time-kill assay.

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Roberto Saporetti

Nanoarchitectonics of the M13 phage provides a potent and specific anti-GD2 vector platform for Neuroblastoma Therapy

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Neuroblastoma (NB) is one of the most common pediatric neuroendocrine tumors, and accounts for 15% of all pediatric cancers. Gangliosides are modified sphingolipids that are abundantly expressed in many cancer cells and relatively very low expressed in healthy tissues. Gangliosides GD2 are extensively expressed on the neuroblastoma cell surface and represent attractive targets for the development of targeted therapies.

Here we used an orthogonal approach (genetic/chemical) to target GD2 with an engineered M13 filamentous phage vector (Figure 1). In particular, the M13 phage was refactored ($M13_{GD2}$) to display 14G2a-based single-chain fragment Variable ScFv (Lv-Hv) against Gangliosides GD2. The $M13_{GD2}$ capsid was then covalently conjugated with hundreds of Rose Bengal (RB), via EDC/NHS cross-coupling reaction, without impairing the selective targeting of the vector. [1]

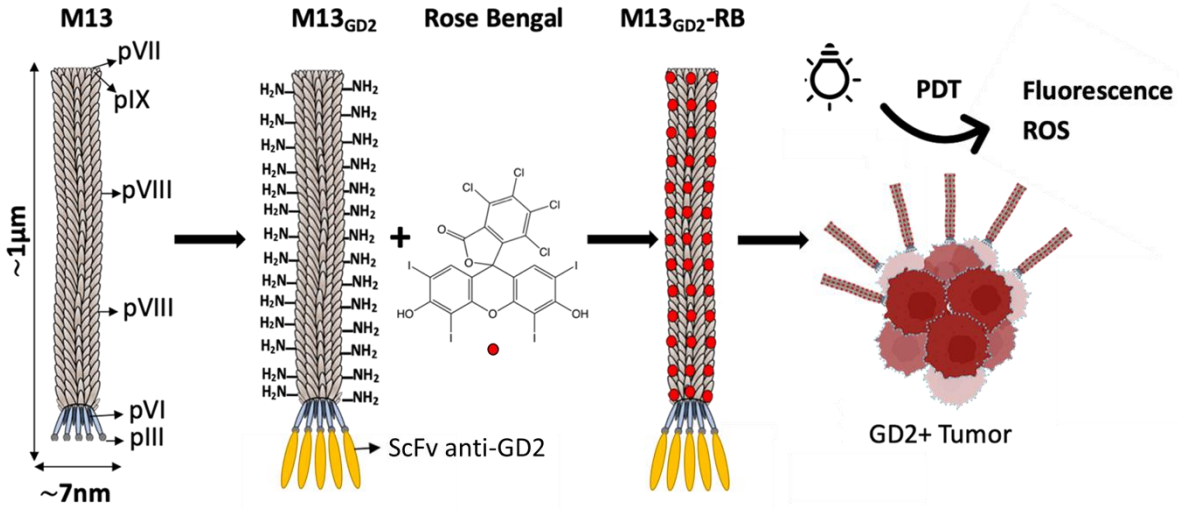

Figure 3: Orthogonal engineering of M13 phage, targeting GD2 positive cell line, for photodynamic therapy (PDT) and fluorescence imaging applications.

$M13_{GD2}$-RB displayed no dark toxicity, while upon irradiation with a low-power white light, $M13_{GD2}$-RB triggered photodynamic death of GD2-positive cells at picomolar concentrations, whereas the GD2-negative cells were unaffected.

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Matilde Tubertini

BODIPYs-carrier Poly-Methyl-Methacrylate Nanoparticles for Photodynamic Therapy

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Photodynamic therapy (PDT) is a minimally invasive and localized method of clinical treatment. By a combination of a special drug called photosensitizer (PS), light and a suitable amount of molecular oxygen, the reactive oxygen species (ROS) are formed, inducing cancer cell death. However some critical issues, such as photosensitizers reduced tumor tissue selectivity and penetration, poor biocompatibility, complex synthetic preparation and difficult chemical modification have limited the use of PDT in clinical oncology.[1] To overcome these limitations, in this work we report, for the first time, the synthesis and characterization of negatively charged core-shall Poly-Methyl-Methacrylate nanoparticles (nPMMA@NPs) electrostatically loaded with modified positively charged BODIPYs (4,4-difluoro-4-bora-3a,4a-diaza-s-indacene). These molecules have recently emerged as promising and easy-to-handle scaffolds for the preparation of effective PDT antitumor agents.[2] The combination of PSs and drug-delivery system lead to better control of selective accumulation in tumor tissues and biocompatibility of PSs; moreover the use of drug-carrier nanoparticles has other advantages, such as overcoming multidrug resistance and preventing enzymatic degradation of active drug.[3] In particular, in this study we focused on the effect on cell viability of BODIPYs-carrier nPMMA nanoparticles on a small panel of 2D- and 3D-cultured human cancer cell lines (e.g. colon cancer cells, HCT116; ovarian cancer cells, SKOV3 and breast cancer cells line, MCF7 and MDA-MB-231), along with their cellular uptake and their ability to induce ROS, apoptosis, necrosis and/or autophagy and to inhibit spontaneous cell migration, compared with free BODIPYs. Our results indicated that nPMMA@NPs reduce cancer cell viability in 3D models of HC116 and MCF7 cells more effectively than the corresponding free compounds. Importantly, we demonstrated that MDA-MB-231 and SKOV3 cell migration ability was significantly impaired by the PDT treatment mediated by nPMMA nanoparticles, likely indicating the capability of this approach to reduce metastatic tumor potential.

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Maria Varsalona

Interaction between Rhodobacter sphaeroides and polydopamine: efficiency of both photosynthetic growth and polymerization.

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Rhodobacter (*R.*) *sphaeroides* is a purple non-sulfur anoxygenic photosynthetic bacteria (APB). The strain R26 is a mutant that lacks carotenoids molecules and contains a smaller photosynthetic apparatus. The photosynthetic apparatus of the strain R26 is formed by an antenna complex (LH1) surrounding the reaction center (RC). RC is the photochemical core of the anoxygenic photosynthesis in bacteria that contains the electron transfer chain (ETC) that initiates the solar driven metabolism of the bacterium.

Dopamine (DA) is a neurotransmitter which polymerizes into polydopamine (PDA), a melanin-like material with excellent adhesive and coatings properties. PDA has been recently explored to improve the extracellular electron transfer from bacteria toward an electrode.

R. sphaeroides in used as model system for several applicative fields, from bioremediation to optoelectronics, focusing specifically on renewable energies. Adaptation of photosynthetic microorganisms at increasing concentrations of DA allows to investigate the effect of the monomer on the cellular vitality of the bacterial strain.

Furthermore, we investigated the photocurrent due to adapted bacteria deposited on glassy-carbon electrode. We demonstrate that DA is not detrimental for the bacterial growth, the cellular morphology, forms a coating layer on the bacterial surface and also produces an increasing photocurrent that is dopamine dependent. Adapted bacteria can represent the active layer of biodevices in bioelectronics, in which both the lifetime and electron transfer from the bacterial RC to the electrode is improved by DA.

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Cesar Vicente-Garcia

Diatom Microalgae as Promising Candidates for the Construction of Robust Biophotovoltaic Devices.

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Biophotovoltaic devices are a promising source of renewable energy, since they can generate electrical current from the photosynthetic activity of microalgae, cyanobacteria, or their isolated proteins. Different strategies such as direct electron transfer or, more commonly, the use of soluble electrochemical mediators allow to directly harvest electrons from photosynthetic organisms' cells and feed them to a closed circuit to generate current. Green microalgae have been extensively studied for the extraction of photocurrent, yielding promising outputs, mainly thanks to their easy culture and fast growth [1]. Alternatively, only a few examples are present in literature about the use of Diatom Microalgae for photocurrent extraction [2].

Besides providing significant photocurrent intensities, diatom microalgae exhibit particular resistance to different kind of stressors such as desiccation, temperature and mechanical pressure, which comes as an advantage when it comes to processing them into a living bioanode [3]. Their sensibility to different contaminants makes them good candidates for the development of electrochemical biosensing devices [4]. Moreover, diatoms hold the unique characteristic of bearing nanostructured biosilica microscopic shells (frustule), that can be functionalized with active molecules or polymers. This opens the door to enhancing electron flow, through conductive polymers [5], or light absorption modulation, for example via introduction of external antennae [6]. This work aims to study the photocurrent extraction from different species of diatom microalgae deposited onto ITO used as working electrode in a three-electrode cell, evaluate their interaction with the electrode and mediator, and their resistance to the electrochemical process itself, particularly in contrast to that of a model green algae. Cyclovoltammetry and chronoamperometry measurements have been performed; both optical and fluorescence microscopies have been used to study the microalgae's state under the different conditions studied. Up to this point, we have standardized a method that allows to produce bioanodes resistant to desiccation, from several different species of diatoms, that provide significant levels of power output.

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Sonja Visentin

Mucins as potential biomarkers for early detection of cancer and as drug delivery systems for PDT

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Mucins are a family of long polymeric glycoproteins. Alterations or overexpression of mucins are associated with mucus-related disorders [1]. Over the last decades, mucins have also been given the status of biomarkers of adverse prognosis becoming an attractive therapeutic target. Gastric carcinoma, pancreatic, colon and rectal, breast, and ovarian cancer have been investigated looking for the roles played by mucins. [2] The early diagnosis is a key factor for outcome, treatments, and healthcare. Thus, the identification and detection of specific and sensitive biomarkers has become of crucial importance. Here we present a spectrophotometric method for the detection of mucin in biological samples (Fig.1a)

Mucins could be considered also natural biopolymers and could be used for the synthesis of mucin-based nanoparticles (Mucosomes) to encapsulate bioactive molecules whose therapeutic efficacy would increase if they were administered in a targeted manner. [3] We encapsulated in mucocosomes a Squaraine dye (SQ), a photosensitizer capable of rapidly releasing reactive oxygen species (ROS). [4] Despite these intriguing features, its use in photodynamic therapy (PDT) is still limited by its chemical instability and self- aggregation traits in biological environments. Preliminary results on the photodynamic activity of the complex Mucosomes-SQ will be presented (Fig.1b)

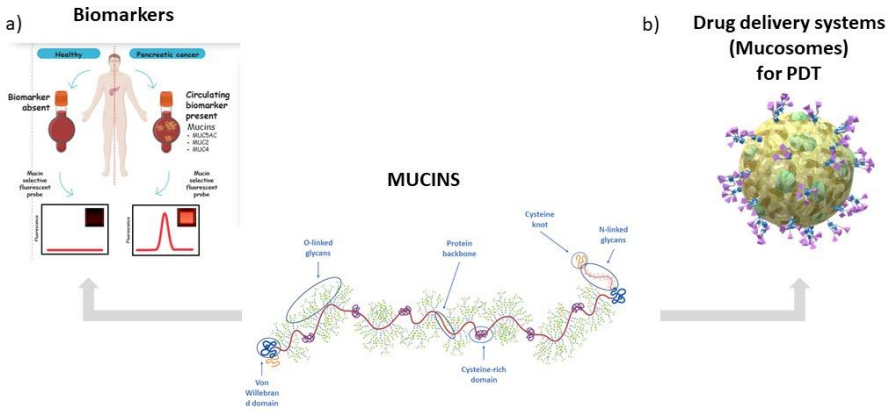

Figure 1

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Poster Communications

Mariafrancesca Coccimiglio

Carbon-Nanoparticles: from waste materials to photo-applications

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The electronic and optical features so far observed for carbon-nanostructures encourage the investigation on these innovative, functional, bio-compatible and eco-sustainable materials, focusing the attention on the development of green synthesis procedures, in the frame of circular economy, starting from waste biomass.[1] In particular, for their wide potential photoinduced application in different fields, from biology to technology, it's useful tuning the photochemical and photophysical features of carbon nanoparticles (CNPs) and this is possible thanks to CNPs easiness of processing with high precision, nanometric size and the possibility to be functionalized through sustainable procedures. Further, protocols with low environmental and energy impact can be designed exploiting waste materials as carbon source. In this contribution, indeed, various bio-waste and by-products, such as coffee grounds and coffee silver-skins, were used as carbon sources. [2] CNPs were thus obtained by means of simple, cheap and ecological hydrothermal synthesis procedures according to an oxidation process. The obtained CNPs were characterized by various spectroscopic techniques including, UV-Visible absorption fluorescence, FT-IR, Raman and XRF spectroscopy. CNPs morphology, instead, was investigated by means of Atomic Force Microscopy (figure 1). The synthesized CNPs have been investigating as photocatalysts for water oxidation processes and as photosensitizers for photodynamic therapy applications.[3]

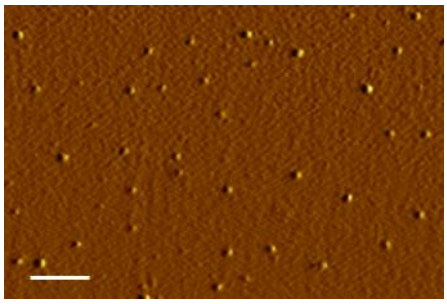

Figure 1. AFM image of the CNPs from coffee-ground synthesis. The bar in the figures is 0.5µm wide.

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Angelo De Paolis

Effects of $Cs_2AgBiBr_6$ Perovskite panels covering the in-door green-house on seed germination and chlorophyll content in *Solanum lycopersicum* L.

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The possibility of exploiting the sunlight to generate electricity, while at the same time allowing the healthy growth of plants (also protecting them from the harmful excess of light), is obtained by covering the greenhouses with semi-transparent solar panels. Perovskite-based halide solar cells appear to be the ideal candidate to achieve this goal [1]. Furthermore, lead-free perovskite can even be an environmentally friendly solution.

In this work, we report on the preliminary data concerning the influence of the lead-free $Cs_2AgBiBr_6$ perovskite, used as active layer for solar cells panels, covering the in-door green-house, on the parameters of germination, development, and chlorophyll content of tomato (*Solanum Lycopersicum* L.) species. The experiments were carried out "in-door" in a growth chamber with controlled conditions of light and temperature, using mini green-houses covered by transparent glass panels placed on the control green-houses (P-), and semi-transparent panels, constituted by glass covered by indium tin oxide (substrate) and $Cs_2AgBiBr_6$ perovskite layers, on the sample (P+).

Axenic seeds of tomato were selected for uniform size and shape, sown in 2 glass Petri dishes (20/dish) containing 3MM paper soaked in water and placed inside two different mini green-houses. After five days tomato germinated seeds were 17/20 either for P- or P+ indicating that different light exposure did not influence tomato germination. The first true leaves (10 mg) of each tomato plant were picked up for chlorophyll extraction and analysis. The average of total chlorophylls (a+b) in control (P-) plants was 1.08 (±0.24) mg/g FW compared to 2.04 (±0.39) mg/g FW in (P+) plants. The chlorophyll content of control plants was in the range reported for healthy plants grown in field conditions. The observed increase detected in (P+) plants was likely due to the plant response to the presence of the Perovskite "screen" lowering the light reaching the plants. The evaluation of plant growth in terms of fresh weight will be also correlated with chlorophyll content.

These results are encouraging for the development of the agrivoltaic solutions based on the semi-transparent solar panel on the greenhouse roofs.

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Nela Malatesti

Photoinactivation of *Legionella pneumophila* in municipal wastewater with two tetracationic porphyrins

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Legionella pneumophila, a Gram-negative bacterium and member of the group of waterborne opportunistic premise plumbing pathogens (OPPPs), can cause serious lung infections, known as Pontiac disease, or life-threatening pneumonia, called Legionnaires' disease. *L. pneumophila*'s main habitat is natural waters and soils, where this bacterium can survive and multiply even under low nutrient and oxygen conditions, high temperatures and is resistant to many antibiotics and disinfectants [1]. The under-explored occurrence of *Legionella* in wastewater treatment plants also poses a serious threat to public health [2]. In our previous work, complete eradication of *L. pneumophila* with photoactivated tetracationic pyridinium-3-yl porphyrin (TMPyP3) was achieved, as well as inhibition of adhesion to polystyrene, and destruction of the biofilm in waters of varying hardness [3]. Metal complexation of porphyrins often increases their chemical stability, and chelation with metal ions such as Zn(II) can promote intersystem crossing, leading to an increased lifetime of the triplet excite state and singlet oxygen ($^1O_2$) production [4], which in turn could be useful for water disinfection applications.

Municipal wastewater poses a possible challenge for photodynamic inactivation (PDI) due to the presence of organic matter, suspended solids and dissolved minerals. In our study of the influence of Zn(II) chelation and different wavelength irradiation on PDI against *L. pneumophila* in municipal wastewater, spectroscopic properties and stabilities of TMPyP3 and its Zn(II) complex (Zn(II)-TMPyP3) were evaluated, as well as their $^1O_2$ production. Antimicrobial activity was investigated using violet light (394 nm, 20 mW/cm^2), from the wavelength range known by the term violet-blue light (VBL), which is also used as a standalone disinfectant, and orange light (607 nm, 2 mW/cm^2), a wavelength corresponding to the absorption spectra of both porphyrins. The results obtained by exposures to single wavelength, as well as the application of different combinations with both wavelengths will be presented.

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Giorgia Miolo

Photostability of a therapeutic monoclonal antibody, Nivolumab-Opdivo®, in its formulation and saline or glucose solutions for parenteral administration.

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Monoclonal antibodies (mAbs) have rapidly escalated as biopharmaceuticals into cancer treatments in these last years, mainly for their target specificity and stimulation of reliable anti-tumoral responses [1]. During their real-life, they are potentially unstable macromolecules under shaking, temperature fluctuations, humidity, and indoor and outdoor light exposure. All these stressors can occur throughout all stages of mAbs production, storage, handling, and administration. It is important to highlight that the physical and chemical modification of mAbs can lead not only to the loss of their bioactivity, but also to the enhancement of their immunogenicity with increasing risks of severe hypersensitivity reactions. Additionally, mAbs administered intravenously are diluted in 0.9% NaCl or in 5% glucose solutions and consequently the excipients are diluted too decreasing their specific role of protection, i.e., against light modifications. The physico-chemical properties and the rate of formation of non-native aggregates are therefore possibly influenced [2]. The photostability of Nivolumab, the active principle of Opdivo ®, a medicine used to treat adults with a type of lung cancer called squamous non-small cell lung cancer (NSCLC) has been studied. The modifications and the biological activity after the light stressor are here reported, with particular attention on the diluting solutions used for its administration to patients.

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Martina Mušković

Amphiphilic cationic tripyridiniumporphyrins and their Zn(II) complexes: the influence of the irradiation wavelength and the length of the alkyl chain

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Amphiphilic porphyrins are increasingly proving to be effective photosensitizers (PSs) and promising for the use in photodynamic therapy (PDT) [1]. In our previous research, cationic porphyrins conjugated with a long alkyl chain (18C) showed much higher cytotoxicity on different cell lines compared to a hydrophilic analogue with an acetamido group [2]. Chelation with zinc(II) ion is expected to increase the lifetime of the triplet excited state (^{3}PS*) and improve singlet oxygen production [3]. Since chelation reduces the number of Q bands from four to two with negligible absorption above 610 nm, activation of Zn(II) porphyrins with red light common to PDT is unlikely to be effective, while orange light is much better suited to their optical properties, which still penetrates tissue relatively well.

We will present the preparation of free-bases and Zn(II) complexes of *N*-methylated tripyridinium-3-ylporphyrins conjugated with alkyl chains of different lengths (1C, 8C-18C) and a study of the influence of their lipophilicity on PDT activity against melanoma cell lines. This study includes the determination of photophysical and photochemical properties in different solvents using various spectroscopic methods (UV-VIS and fluorescence spectroscopy, laser flash photolysis (LFP) and time-resolved fluorescence spectroscopy (TRF)) as well as *in vitro* biological analyses on two different melanoma cell lines (A375 and MeWo) and human dermal fibroblasts (HDF), where cellular uptake of each PS, its intracellular localisation and cytotoxicity were investigated. In addition, the MTT assay was used to compare the application of two different wavelengths for photoactivation of the PSs, red (645 nm; 2.0 mW / cm^2) and orange light (607 nm; 2.0 mW / cm^2).

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Massimo Trotta

Do photosynthetic bacteria dream of electrode surfaces?

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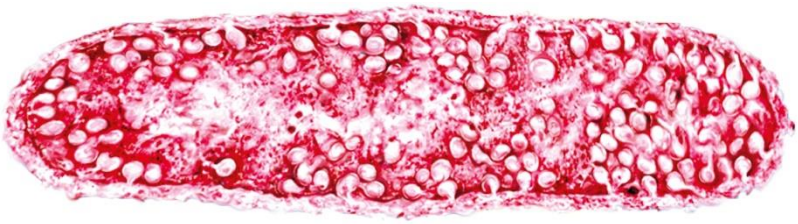
Photosynthetic bacteria are a class of microorganisms that have shown great potential for energy transduction processes, including biophotovoltaic applications. To be effective they require the use of electrodes capable to ensure electron conduction with the bacterial cell wall, without jeopardizing the surviving of the biological entities.



A new class of self-standing electrodes based on carbonaceous material have shown great electrical properties and great biological compatibility. These electrodes will be presented as innovative electron transfer component in biophotovoltaics.

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Marina Venturini

Photodynamic therapy with Zn(II) phthalocyanine (RLP068/Cl) for hidradenitis suppurativa.

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Several studies have been published since 2004 on the use of photodynamic therapy (PDT) to treat hidradenitis suppurativa. The use of superficial or interstitial illumination with 5-amino-levulinic acid (5-ALA) or methylene blue (MB) have been proposed. Injecting 5-ALA or MB followed by illumination with a fiber optic sensor placed inside the lesion appears to be a better method of treating these thick lesions. A novel photosensitizer, called RLP068/Cl, is a tetracationic Zn(II)phthalocyanine derivative that have demonstrated a good efficacy against surgical wound infections induced by a methicillin-resistant strain of Staphylococcus aureus and also against prosthetic joint infections-associated biofilms induced by Pseudomonas aeruginosa. We evaluated the efficacy and safety of topical PDT with RLP068/Cl 0.3% in gel formulation on 17 patients with hidradenitis suppurativa (HS), irradiated with red LED light source at 630 nm for 8 min (120 mW/cm corresponding to 60 J/cm2 of delivered light dose). The treatment was delivered twice a week for 6 weeks. A complete response was obtained in 47% of treated patients with resolution of inflammed lesions (nodules, abscesses), reduction of draining tunnels and improvement of pain and itch symptoms. The treatment was well tolerated without side effects. PDT with RLP068/Cl represent an interesting therapeutic option in the landscape of the future treatment of HS as monotherapy for mild HS or in association with biologics for moderate-severe HS.

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Marina Venturini

Field validation of a satellite-based dosimeter of personal solar exposure.

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The results of a field study validating a novel satellite-based digital solution for personal solar exposure dosimetry ("ExpoDose" by siHealth Ltd, UK) will be presented. A mobile app tracking the user's position and satellite data processing are used for providing up-to-date personal solar dosimetry data for any action spectrum (e.g., erythema, vitamin D synthesis, DNA damage) and different body sites via a dedicated web-portal. The app is autonomous and requires no external sensors neither direct exposure of the smartphone to sunlight since solar radiation is monitored from satellite (i.e. smartphone can be kept in a pocket). This digital solution is enabled by the HappySun® satellite-based technology for near real-time monitoring of solar irradiance worldwide (already scientifically validated in multiple studies) and by an automatic outdoor position detection technology based on AI models applied to smartphone sensors data.

These two technologies combined allow the remote monitoring of solar dose with 1 minute resolution for any number of users, multiple action spectra and multiple body sites simultaneously. Data collected with the ExpoDose system were compared to 10 high-quality wearable UV electronic dosimeters (Scienterra Ltd, New Zealand) measuring irradiance on 10 measurement planes oriented over a range of 4 different zenith angles and 8 compass points. The wearable dosimeters were calibrated with a research standard UV-erythemal radiometer (Kipp & Zonen, Netherlands) installed horizontally. Data were collected during spring and summer in Harwell Campus (Oxfordshire, UK) and in Brescia (Italy). Preliminary results show a high accuracy of the satellite-based solar dosimetry system, yielding an R^2 correlation coefficient of 0.90 and a mean absolute error (MAE) of 21% on the horizontal plane. Moreover, the automatic outdoor detection component has been tested in a broad range of scenarios on smartphones running both Android and iOS operating systems. Using cross-validation techniques over multiple smartphone models, detection accuracies resulted over 92% on Android and 84% on iOS. A remote personal solar monitoring system has great promise for use in multi-participatory studies that need to account for personal solar exposure levels of study subjects. Carefully calibrated and maintained high-quality solar dosimeters have been demonstrated to have an estimated error of 12%. Compared to remote personal dosimetry, they are costly, require expertise to maintain and calibrate and require high levels of attention and compliancy from experiment subjects. So, the ExpoDose system can be effectively used for research and clinical studies, replacing the need for costly and time-consuming physical dosimeters in multi-participatory longitudinal solar exposure studies.

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