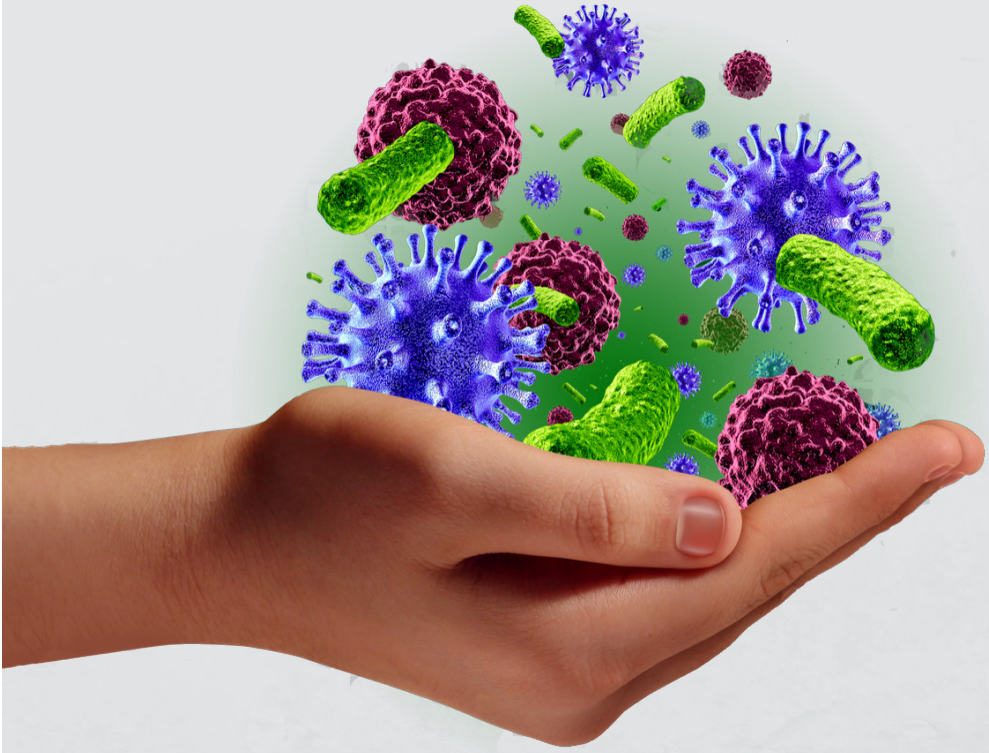
Rome
January 14- 16, 2026



Book of Abstracts

ICONAN 2026

Bridging BASIC BIO-NANO-SCIENCE
and CLINICAL TRANSLATION

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Eric Appel [1]

1. *Stanford University*

TBA

A nanoparticle platform towards gut hormone stimulation in the treatment of gastrointestinal disorders

Wednesday, 14th January - 09:40: Plenary Session 1 (Auditorium) - Plenary Speaker - Abstract ID: 315

Ana Beloqui [1]

1. *Université catholique of Louvain*

TBA

Insights into Nanomaterials-Bio Interactions from Simulations and Theory

Wednesday, 14th January - 10:50: Plenary Session 2 (Auditorium) - Plenary Speaker - Abstract ID: 319

Alfredo Alexander-Katz [1]

1. *MIT*

TBA

On the design of supramolecular therapeutics

Wednesday, 14th January - 11:30: Plenary Session 2 (Auditorium) - Plenary Speaker - Abstract ID: 313

Giuseppe Battaglia [1]

1. *Institute for Bioengineering of Catalonia (IBEC)*

TBA

Entropy-Driven Multi-Scale AI Model for Nanoparticle–Immune Interaction Prediction

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 304

Xuan Khanh Truong [1], ***Quynh Hoa Truong*** [1]

1. *PhD Scholar*

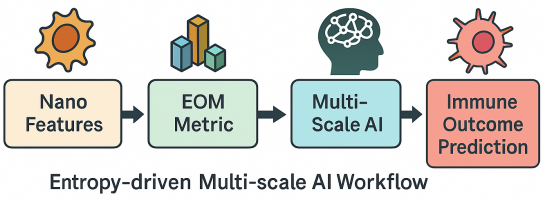
Entropy-Driven Multi-Scale AI Model for Nanoparticle–Immune Interaction Prediction

Precise control of how nanomaterials interact with the immune system remains one of the major challenges in nanomedicine. Small variations in nanoparticle size, surface chemistry, protein-corona transitions, and mechanobiological conditions can lead to disproportionate changes in cellular uptake, immune recognition, and therapeutic efficacy. Existing computational approaches often treat these biological processes independently, limiting their predictive and translational relevance.

We introduce an entropy-driven, multi-scale AI framework that integrates nanoscale physicochemical descriptors, corona-evolution dynamics, cellular mechanobiology, and immune-activation signatures into a unified predictive model. Central to the methodology is the Entropy-Oriented Interaction Metric (EOM), which quantifies configurational uncertainty and microstate imbalance at the nano–bio interface. These entropy-derived descriptors are embedded within a machine-learning architecture capable of capturing multi-scale coupling and stochastic interaction behaviors.

Using publicly available nano–bio interaction datasets, the framework is benchmarked across phagocytic clearance, tumor penetration, and tissue-specific uptake conditions. Incorporation of entropy-based descriptors significantly improves predictive accuracy, calibration stability, and inter-dataset generalization compared with classical physicochemical models. Design-space exploration further reveals nanocarrier configurations that minimize immune activation while enhancing targeted delivery in cancer and inflammatory environments.

This work provides an interpretable, AI-driven platform for predictive nano–immune modeling and precision delivery engineering. The proposed framework supports personalized nanocarrier optimization, accelerates rational design, and offers transferrable mechanistic insights for next-generation nanotherapeutics.



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Modulating Blood-brain barrier low-density lipoprotein receptor-related proteins (LRP) receptors using multivalent drugs.

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 266

Marco Basile [1], ***Cátia Lopes*** [1], ***Valentino Barbieri*** [1], ***Matilde Ghibaudi*** [1], ***Jose Muñoz*** [1], ***Vanina Cosenza*** [1], ***Lorena Ruíz Perez*** [1], ***Giuseppe Battaglia*** [1]

1. *Institute for Bioengineering of Catalonia (IBEC)*

Neurodegenerative diseases, such as Alzheimer's disease (AD), represent a major health challenge, with limited therapeutic options available primarily due to the difficulty of delivering treatments effectively across the blood-brain barrier (BBB). One hallmark of Alzheimer's disease (AD) pathology is the accumulation of amyloid-beta (Aβ) peptides in the brain parenchyma, driven in part by impaired BBB clearance mechanisms. The low-density lipoprotein receptor-related proteins (LRP) receptors, particularly LRP1 and LRP8, play crucial roles in the receptor-mediated transcytosis and clearance of Aβ peptides across the BBB. Hence, enhancing receptor-mediated transport represents a promising therapeutic strategy.

In this study, we utilized biodegradable and biocompatible poly(ethylene glycol)-poly(lactic acid) (PEG–PLA) micelles to investigate their potential in promoting brain barrier (BBB) transcytosis of Aβ peptides. We specifically explored the concept of multivalent super-selectivity, a phenomenon whereby nanoparticle avidity significantly enhances specific interactions with targeted receptors on brain endothelial cells (BECs). By carefully tuning the ligand density on PEG–PLA nanoparticles, we achieved precise control over nanoparticle avidity, which is crucial for selectively promoting transcytosis over endocytosis.

Binding assays conducted in vitro demonstrated distinct binding patterns based on ligand specificity, highlighting the importance of the ligand in nanoparticle-BEC interactions. Meanwhile, permeability assays identified formulations capable of efficient transcytosis. Gene and protein expression analyses further validated the potential therapeutic effect, revealing modulation of key BBB-associated biological markers. In parallel, our investigations into receptor dynamics demonstrated differential interactions of LRP1 and LRP8 with intracellular mediators Rab5 and PACSIN2 upon exposure to Aβ40 and Aβ42 assemblies. These findings revealed novel insights into receptor-specific clearance pathways, identifying LRP8 as a promising new target for Aβ clearance.

Overall, our study demonstrates the significant potential of multivalently functionalised PEG–PLA nanoparticles to selectively enhance receptor-mediated transcytosis at the BBB. This strategy not only improves our understanding of transcytotic mechanisms but also provides a robust framework for developing effective nanotherapeutics aimed at mitigating neurodegeneration in Alzheimer's disease and other related conditions.

Polyhistidine-functionalized magnetic nanoparticles enhancing intracellular heating efficiency in magnetic hyperthermia

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 240

Ludivine TRIZAC-MATTERN [1], ***Tieu Ngoc Nguyen*** [1], ***Mélody Perret*** [1], ***Aude Michel*** [1], ***Fabienne Burlina*** [2], ***Emilie Secret*** [1]

1. *Sorbonne Université, CNRS, Physicochimie des Électrolytes et Nanosystèmes Interfaciaux (PHENIX), 4 place Jussieu, Paris, 75005 France,* ***2.*** *Sorbonne Université, École Normale Supérieure, PSL University, CNRS, Chimie Physique et Chimie du Vivant (CPCV), 4 place Jussieu, Paris, 75005 France*

Magnetic nanoparticles (MNPs) are powerful tools in nanomedicine for localized cancer therapy via magnetic hyperthermia. Indeed, when exposed to an alternating magnetic field, MNPs convert magnetic energy into heat, which leads to thermal damage and can enhance chemotherapeutic efficiency. Their therapeutic action, however, is often limited by endosomal entrapment and aggregation after internalization, which significantly reduces their heating capacity. [1] Overcoming this intracellular confinement is therefore crucial to exploit their potential in cancer therapy.

To address this limitation, we designed γ-Fe_2O_3@SiO_2 core-shell nanoparticles with an outer silica layer that allows versatile surface functionalization. Sulfo-betaine zwitterions were also added to the surface to promote colloidal stability and stealth. Histidine-rich peptides were then grafted onto the surface to promote endosomal escape via the proton sponge effect, enabling the nanoparticles to reach the cytosol and recover their magnetic mobility and heating efficiency.[2]

Preliminary characterizations confirm the synthesis of monodisperse γ-Fe_2O_3 cores coated with silica shells and successful conjugation of polyhistidine peptides. Confocal microscopy studies demonstrated effective endosomal escape and cytosolic distribution of these functionalized nanoparticles in SH-SY5Y neuroblastoma cells. Magnetic hyperthermia experiments are being performed on the same cell line (SH-SY5Y) to correlate nanoparticle localization with heating efficiency and cellular viability, providing insights into the relationship between intracellular diffusion and thermal response.

Future work aims to induce further cell death by including synergistic effects by adding chemotherapeutic agents (doxorubicin) or gene silencing siRNAs. The inhibition of certain genes is expected to sensitize tumor cells to thermal damages and enhance treatment efficacy. Combining these gene-silencing effects with the localized heating could lead to a significant increase in apoptotic cell death.

1. Di Corato, R. *et al.* Magnetic hyperthermia efficiency in the cellular environment for different nanoparticle designs. *Biomaterials* **35**, 6400–6411 (2014).

2. Perret, M. *et al.* Intracellular Proteins Targeting with Bi-Functionalized Magnetic Nanoparticles Following their Endosomal Escape. *Small* **21**, 2410454 (2025).

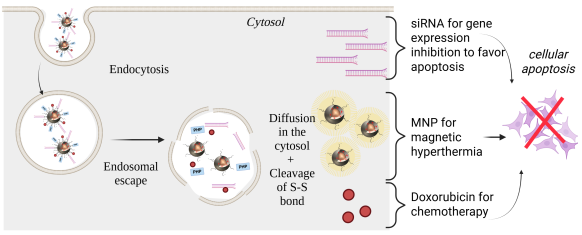

Figure: Illustration of the action of peptide functionalized MNPs for effective magnetic hyperthermia coupled to chemotherapy and gene silencing.

Figure action of peptide functionalizednps trizac-mattern.png

Advanced 3D-Printed Tablets for Iron Supplementation: Functionalized Nanoparticles for Enhanced Bioavailability and Therapeutic Efficacy

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 168

Isadora Florêncio de Souza [1], ***Mac-Kedson Medeiros Salviano Santos*** [2], ***Alexandre Silva Santos*** [3], ***Ariane Pandolfo Silveira*** [4], ***Diego Sousa-Moura*** [5], ***Idejan Padilha Gross*** [6], ***Ingrid Gracielle Martins da Silva*** [1], ***Luis Alexandre Muehlmann*** [2], ***Marcílio Sérgio Soares da Cunha Filho*** [6], ***Sebastião William da Silva*** [3], ***Sônia Nair Báo*** [1], ***Marcelo Henrique Sousa*** [2]

1. *Electron Microscopy Laboratory, Cell Biology Department, Institute of Biological Sciences, University of Brasilia, Brasília, Distrito Federal, 70910-900, Brazil,* ***2.*** *Green Nanotechnology Group, University of Brasilia, CEP 72220-900, Brasilia-DF, Brazil,* ***3.*** *Optical Spectroscopy Laboratory, Institute of Physics, University of Brasília, Brasília-DF, 70910-900, Brazil,* ***4.*** *Electron Microscopy Laboratory, Cell Biology Department, Institute of Biological Sciences, University of Brasilia, Brasília, Distrito Federal, 70910-900, Brazil;,* ***5.*** *Laboratory of Nanobiotechnology, Department of Genetics and Morphology, Institute of Biological Sciences, University of Brasilia, Brasilia, Distrito Federal, 70910-900, Brazil,* ***6.*** *Laboratory of Food, Drug, and Cosmetics (LTMAC), School of Health Sciences, University of Brasilia, 70.910-900 Brasília, DF, Brazil*

Iron deficiency is one of the most prevalent nutritional disorders worldwide, particularly affecting children and women, and can lead to anemia in severe cases. Conventional treatments, based on oral or intravenous iron supplementation, present significant drawbacks such as low bioavailability, uncontrolled release, and gastrointestinal side effects. In this context, the integration of nanotechnology with three-dimensional (3D) printing has emerged as an innovative strategy to enhance therapeutic efficacy through precise modulation of drug release, individualized dosing, and minimization of adverse effects. This study proposes the development of 3D-printed tablets containing iron oxide nanoparticles (IONPs) as an advanced platform for iron supplementation, aiming to overcome the limitations of conventional formulations. IONPs were synthesized via co-precipitation of iron ions solution, subsequently functionalized with citrate and dispersed in glycerol to improve bioavailability and enable the 3D printing process. The nanoparticles were incorporated into filaments by hot-melt extrusion and used to fabricate 3D-printed tablets via Fused Deposition Modeling (FDM). Physicochemical characterization included colloidal stability analysis, X-ray diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), morphological assessment, dissolution studies in simulated gastrointestinal fluids, and toxicity evaluation using zebrafish embryos. Four nanoparticle variants were synthesized: uncoated IONP, citrate-coated IONP (IONP@Cit), IONP dispersed in glycerol (IONP_gly), and citrate-coated IONP dispersed in glycerol (IONP@Cit_gly), along with their respective printed formulations (IONP3D, GIONP3D, CIONP3D, and CGIONP3D). Uncoated particles showed size increase under alkaline conditions, whereas citrate-functionalized nanoparticles displayed greater stability, and glycerol dispersion further enhanced colloidal behavior. FTIR and XRD confirmed the successful synthesis of pure iron oxide and effective surface functionalization. Electron microscopy revealed spheroidal particles averaging 10–300 nm and the presence of IONPs within the 3D-printed matrices. The CGIONP3D formulation exhibited superior dissolution under alkaline conditions compared to GIONP3D, indicating improved dispersion due to surface coating. Biological assays in zebrafish embryos demonstrated IONP adhesion to the chorion without significant alterations in hatching or embryonic development, confirming a low-toxicity profile. Similarly, IONP@Cit_gly showed slightly delayed hatching but no developmental abnormalities. Therefore, our study demonstrates the versatility of iron oxide nanoparticles in 3D-printed tablets, offering enhanced dissolution, controlled release, and low toxicity, representing an innovative, effective oral platform for iron supplementation.

1A

	IONP			IONP@Cit			IONP_Gly			IONP@Cit_Gly		
pH	Size	PDI	ZP	Size	PDI	ZP	Size	PDI	Zeta	Size	PDI	ZP
2.5	471.53	0.61	27.00	1525.33	0.39	6.84	197.17	0.45	33.13	4042.00	0.144	11.43
7.2	874.10	0.33	19.37	257.17	0.538	-26.37	1638.00	0.19	17.47	116.20	0.299	-43.17
11.5	913.40	0.56	-27.33	368.87	0.628	-36.33	212.57	0.54	-36.63	115.93	0.341	-36.93

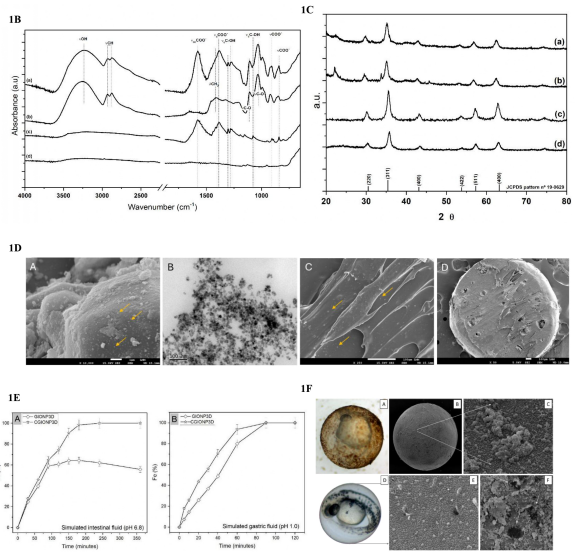

Figure 1. **(1A)** Colloidal parameters of nanoparticles: size, polydispersity index (PDI), and zeta potential (ZP) at different pH values. **(1B)** FTIR spectra of iron oxide nanoparticles: (a) IONP@Cit_gly; (b) IONP_gly; (c) IONP@Cit; (d) IONP. B. **(1C)** Diffraction patterns of the different printlets formulations: (a) GIONP3D; (b) CGIONP3D compared to (c) pure iron oxide nanoparticles (IONP) and (d) citrate-coated iron oxide nanoparticles (IONP@Cit). **(1D)** SEM and TEM morphological analysis. Colloidal suspension of pre-processed IONPs (before extrusion and printing) obtained via SEM (A) and TEM (B). Surface of the 3D-printed material, indicating the presence of IONPs distributed throughout the structure of the tablet (C). Representation of the extrudate (used in tablet printing) at 250x magnification (D). **(1E)** Dissolution profiles of GIONP3D and CGIONP3D printlets under simulated conditions of (A) intestinal pH (6.8) and (B) gastric pH (1.0). **(1F)** Zebrafish embryos analyzed by optical microscopy and SEM. A: Optical image showing IONPs adhered to the chorion. B: SEM of an embryo covered with IONPs (75×). C: IONPs distributed on the chorion (5000×). D: Optical image of an embryo without IONP exposure. E: SEM of the chorion surface without IONPs (5000×). F: SEM of the chorion exposed to IONPs, showing nanoparticles dispersed around pores (arrows).

Advanced 3d-printed tablets for iron supplementation functionalized nanoparticles for enhanced bioavailability and therapeutic efficacy.jpg

Mimicking Collagen Fibrils through Hyperstable Short Collagen-Mimetic Peptide Assemblies

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 127

Smriti Mukherjee [1], ***Vijayakumar Varshashankari*** [2], ***Ashokraj Sundarapandian*** [2], ***Niraikulam Ayyadurai*** [2], ***Ganesh Shanmugam*** [1]

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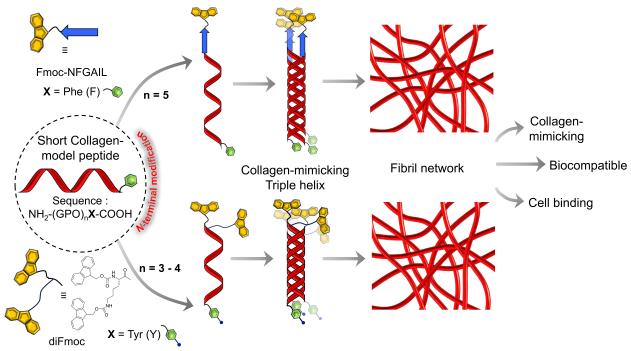
Collagen, the most abundant fibrous protein in mammals, possesses a characteristic triple-helix structure that governs tissue mechanics and cellular growth. Its excellent biocompatibility has made it indispensable in tissue engineering, particularly in wound healing. However, animal-derived collagen, widely used in biomedical applications, suffers from batch variability, pathogen risk, and immunogenicity. Collagen-mimetic peptides (CMPs), composed of Gly-Pro-Hyp (GPO) repeats, offer a synthetic alternative. Yet, most CMPs require long sequences ($\geq$9 GPO repeats) to form fibrils, making large-scale production and purification difficult. A key challenge is to design short CMPs that not only stabilize the triple helix but also assemble into fibrillar nanostructures capable of effective biological interfacing.

Here, we present CMP-based nanofibrils as a new class of biomimetic nanomaterials for nanomaterial–body interactions. Using two molecular design strategies, we developed short CMPs ($\leq$6 GPO repeats) that self-assemble into stable triple helices and form fibrillar networks. In the first strategy, $(GPO)_5$ was modified with a π-capped amyloid hydrogelator sequence (Fmoc-NFGAIL) at the N-terminus and phenylalanine at the C-terminus. This construct formed triple helices (T_m = 35 °C) that further assembled into dense fibrillar networks resembling collagen. These fibrils exhibited strong biocompatibility, supporting fibroblast adhesion. In the second strategy, CMPs with 3–6 GPO repeats were double-Fmoc capped at the N-terminus and tyrosine at the C-terminus. These diFmoc-capped CMPs formed highly stable triple helices (T_m up to 76 °C) with rapid folding, providing production advantages over both native collagen and conventional CMPs. Additionally, this strategy reduced the number of GPO repeats required for triple-helix formation to three, the lowest reported to date. The resulting nanofibrils promoted fibroblast adhesion and proliferation, driven by receptor recognition of the triple-helical motifs and fibrillar networks.

Together, these studies establish CMP-derived nanofibrils as multifunctional nanomaterials at the bio–nano interface. By mimicking native collagen, they actively engage with cells, enhancing adhesion and proliferation, while offering a modular platform where peptide sequence and aromatic capping can be tuned for therapeutic outcomes. These results highlight CMP-based nanofibrils as promising next-generation biomaterials for nanomaterial–body interactions, wound healing, regenerative medicine, and future disease-specific applications.



Graphical abstract.png

Copper oxide nanoparticles as delivery vehicles for different Pt(ii)-drugs: experimental and theoretical evaluation

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 97

Shahdan Abdelkareem [1], ***Mayyada El-Sayed*** [1], ***Aly Reda*** [1], ***Nahed Yacoub*** [1], ***Valeria Butera*** [2], ***Matteo Camellone*** [3], ***Ida Ritacco*** [4], ***Tamer Shoeib*** [1]

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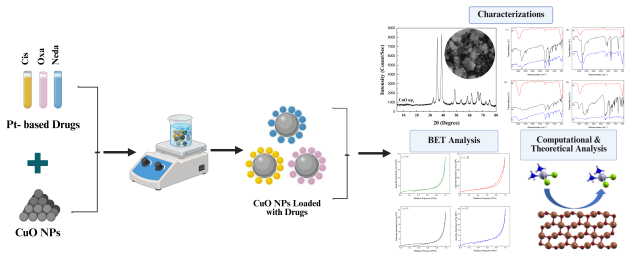
Chemotherapy is a key element in cancer treatment. The first drugs to be clinically used for this purpose were platinum(II) complexes and even today they are highly effective in the treatment of the disease. However, side effects, resulting from their use, limit their clinical usefulness. Furthermore, if administered intravenously into the circulation, platinum(II)-based anticancer medications may cause adverse effects due to interactions with molecules found in human bodies, thus preventing them to reach the final target. Stomach secretions can also destroy them. As a result, their absorption might be restricted, rendering oral delivery ineffective. Over the years, several methodologies were developed to overcome the limits associated with the use of the platinum(II) drugs, including their targeted delivery. In this context, our study proposes copper(II) oxide nanoparticles (CuO NPS) as a promising and excellent carrier of platinum(II)-based anticancer drugs. In this work, we examined the loading efficiency of cisplatin, oxaliplatin and nedaplatin on the surface of CuO nanoparticles by using experimental techniques such as UV-visible spectroscopy, FTIR spectroscopy, the BET method, and XRD, and theoretical ones based on DFT calculations under periodic boundary conditions (PBC). UV-vis spectroscopy determined that cisplatin had the highest entrapment efficiency and loading capacity compared to the other drugs, with 52% entrapment efficacy, indicating a stronger binding with CuO nanoparticles. The experimental results are consistent with DFT simulations indicating that Pt(II)-drugs exhibit favorable adsorption on CuO (111) surfaces, particularly when the Pt(II)-drug is cisplatin. The most stable configurations indicate that cisplatin, nedaplatin, and oxaliplatin prefer to coordinate with the surface tri-coordinated Cu. However, cisplatin has the most intense contact with the copper oxide surface, with an adsorption energy (E_{ads}) of -3.0 eV. Both experimental and theoretical results highlight that CuO nanoparticles are excellent Pt(II) anticancer drug carriers, especially in the case of cisplatin, which undergoes strong interactions with the support, necessary for the delivery phase, and easy desorption, important in the antitumor action phase of the drug.



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Sustainable nanotechnology: Plant-based titanium dioxide nanoparticles for renal cancer radiotherapy

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 54

Mahima Yadav [1], ***Rasika Samarasinghe*** [1], ***Jason Hodge*** [2], ***Terrence Piva*** [3], ***Moshi Geso*** [3], ***Rod Lynch*** [4], ***Bill Patterson*** [5], ***Faiza Basheer*** [1]

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Renal cell carcinoma (RCC) is known for its resistance to radiotherapy, making it a difficult cancer to treat effectively, especially due to the adverse effects associated with high radiation doses. To address these challenges, we report the first synthesis of titanium dioxide nanoparticle (TiO_2 NPs) using Australian native plant extracts, chosen for their rich phytochemical profiles. This green synthesis approach offers a sustainable alternative to conventional chemical methods, with the added benefit of potential biological compatibility.

Comprehensive characterization of the green-synthesized TiO_2 NPs revealed that they are predominantly spherical in shape with an average size ranging from 10–20 nm, as observed by scanning and transmission electron microscopy (SEM and TEM). X-ray diffraction (XRD) analysis confirmed the successful formation of TiO_2 NPs in the pure anatase phase, with characteristic peaks at 2θ = 25.3°, 37.8°, 48.0°, 53.9°, and 55.1°. Dynamic light scattering (DLS) confirmed a stable and narrow size distribution, while thermogravimetric analysis (TGA) displayed thermal stability suitable for biological applications.

FTIR spectroscopy showed strong Ti–O stretching vibrations in the 400–800 cm^{-1} range, with additional peaks at 1630–1660 cm^{-1} corresponding to organic functional groups, suggesting the presence of phytochemical residues acting as natural capping and stabilizing agents.

In vitro studies using the 786-O renal carcinoma cell line showed efficient cellular uptake of the TiO_2 NPs, as visualized under confocal microscopy. The NPs showed high biocompatibility and, when applied as an adjuvant to radiotherapy, they significantly enhanced cancer cell sensitivity to radiation. This enhancement allowed for potential reduction in radiation doses without compromising therapeutic efficacy. Compared to chemically synthesized TiO_2 NPs, the green-synthesized NPs showed superior radiosensitizing effects.

This work highlights the potential of integrating green chemistry with advanced nanotechnology to develop safer and more effective cancer therapies. The promising results of this study provide a strong foundation for further research, including *in vivo* investigations and clinical translation, to establish plant-based TiO_2 NPs as a novel adjuvant for radiotherapy in the treatment of radioresistant cancers such as RCC.

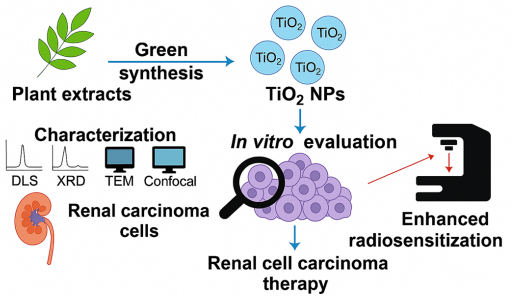

Figure: Schematic representation of the green synthesis of TiO_2 NPs (Titanium dioxide Nanoparticles) using plant extracts, followed by their physicochemical characterization and *in vitro* evaluation as radiosensitizers for renal cell carcinoma therapy.

Renal cell carcinoma radiosensitization.png

Detailed Proteomic Analysis of Protein Corona on Mannose Based Glycopolymers and Their Response in Tumour Microenvironment

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 8

Aneeqa Safdar [1], ***Martina Stenzel*** [1], ***Megan Lord*** [1]

1. *University of New South Wales*

It has been well studied now that tumours endure changes in their cellular metabolism[1]. Tumours require excessive glucose in order to satisfy their vulnerable growth needs.[2]. During the past few years as a family of sugars, mannose is gaining more and more interest because of its tumour supressing capabilities[3, 4]. However, nanoparticles with mannose can target cells, but they are also prone to protein corona formation. Therefore, the content of mannose needs to be carefully finetuned. Here we prepared $PManMA_{47}$-PS_{51}-co-PEO_{44}-PS_{40} micelles with $PManMA_{47}$-PS_{51} ranges from 0% to 100% and observed that micelles size decreases and more shaped with increasing mannose content (~84 nm- 29 nm from 0%-100%). We are interested in if protein profiles changes with changing mannose content in $PManMA_{47}$-PS_{51}-co-PEO_{44}-PSglycopolymer and if there is a relationship between adsorbed proteins on the cellular uptake of healthy (macrophages) and tumour cells with high mannose receptors, and what kind of proteins are adsorbing on these glycopolymers. We found out that although there is no significant difference quantitatively on the number of adsorbed proteins but there are few proteins which are specific to certain mannose ratio. Cytotoxicity and cellular uptake increase with increasing mannose content.

References:

[1] Hanahan, D.; Weinberg, R. A. Hallmarks of cancer: the next generation. *cell* **2011**, *144* (5), 646-674.

[2] Pavlova, N. N.; Thompson, C. B. The emerging hallmarks of cancer metabolism. *Cell metabolism* **2016**, *23* (1), 27-47.

[3] Nan, F.; Sun, Y.; Liang, H.; Zhou, J.; Ma, X.; Zhang, D. Mannose: A Sweet Option in the Treatment of Cancer and Inflammation. *Front Pharmacol* **2022**, *13*, 877543. DOI: 10.3389/fphar.2022.877543 From NLM.

[4] Gonzalez, P. S.; O'Prey, J.; Cardaci, S.; Barthet, V. J. A.; Sakamaki, J.-i.; Beaumatin, F.; Roseweir, A.; Gay, D. M.; Mackay, G.; Malviya, G.; et al. Mannose impairs tumour growth and enhances chemotherapy. *Nature* **2018**, *563* (7733), 719-723. DOI: 10.1038/s41586-018-0729-3.

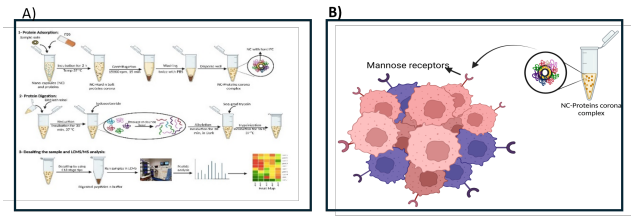

Figure 1 : Schematic Illustration of A) detailed proteomic analysis of micelles by LCMS[2], B) Targeting overexpressed mannose receptors in tumours

Schematic illustration of a detailed proteomic analysis of micelles by lcms2 b targeting overexpressed mannose receptors in tumours.png

Response Surface Optimization of DNA-Lipid Nanoparticles Targeting HPV18 E7: Linking Microfluidic Process Parameters to Physicochemical Attributes and HeLa Cell Viability

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 287

Iria Naveira Souto [1], ***Roger Fabrega Alsina*** [2], ***Carlos J. Ciudad*** [3], ***Elisabet Rosell Vives*** [4], ***Anna Lagunas Targarona*** [5], ***Jessica Malavia*** [6], ***Laia Montell Bonaventura*** [7]

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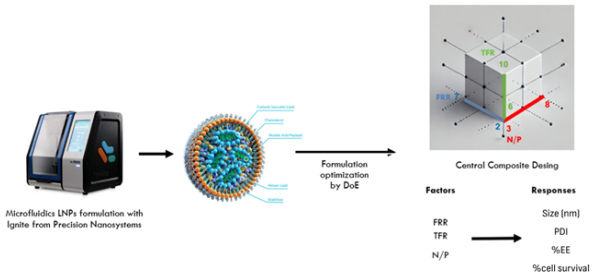
The encapsulation of DNA within lipid nanoparticles (DNA-LNPs) is a promising strategy for targeted gene therapy. Human papillomavirus type 18 (HPV18) encodes the E7 oncoprotein, a key contributor to cervical carcinogenesis. In this work, we developed DNA-LNPs loaded with a polypurine reverse Hoogsteen (PPRH) oligonucleotide targeting the HPV18 E7 oncogene and applied response surface methodology to map their microfluidic fabrication space. A central composite design was implemented to study three process parameters—flow rate ratio (FRR), total flow rate (TFR) and N/P ratio (molar ratio between ionizable lipid nitrogens and DNA phosphates). Four responses were monitored: particle size, polydispersity index (PDI), encapsulation efficiency (%EE) and HeLa cell viability (% viability) measured by MTT assay after treatment with PPRH-LNPs.

ANOVA for %cell survival showed that the quadratic model was highly significant ($p < 0.001$). The N/P ratio emerged as the dominant factor, exhibiting strong linear and quadratic effects ($p < 0.001$), consistent with its central role in governing nanoparticle surface charge and DNA complexation. FRR also contributed significantly through its squared term, whereas TFR and two-factor interactions displayed more modest influences within the explored design space. Standardized Pareto charts highlighted N/P and its quadratic term as the largest effects, followed by the quadratic terms of FRR and TFR. Diagnostic plots identified two runs with large residuals, but the overall model adequately captured the main trends in the data.

In parallel, the same design enabled characterization of how FRR, TFR and N/P shape key physicochemical attributes of the formulation. Within the studied range, nanometric particle sizes with low PDI and high %EE were obtained, indicating that the selected factor space is suitable for gene-delivery applications. A multi-response desirability function was used to jointly target ~75 nm size, low PDI, high %EE and reduced HeLa viability, identifying FRR 3.14, TFR 8.69 and N:P 6.94 ($D = 0.88$) as the optimal compromise. Experimental validation yielded 72.2 nm DNA-LNPs with PDI 0.103 and %EE 99.3%, reducing HeLa viability to 42%. These optimized conditions will delineate a preliminary design space to guide future development of PPRH-based DNA-LNP formulations for HPV-targeted gene therapy.



Naveira iria abstract iconan image.png

Cell Engineering via small EVs in a microfluidic system

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 271

Anna Menale [1], ***Enza Torino*** [1]

1. *University of Napoli Federico II*

Extracellular vesicles (EVs) derived from immune cells have emerged as promising vehicles for immunomodulation and therapeutic delivery, particularly in cancer and inflammatory diseases. Various strategies for EV engineering exist, with promising applications in nucleic acid delivery. THP-1-derived EVs represent a reproducible in vitro model for studying monocyte/macrophage interactions. This study focuses on a microfluidic-centered approach for the generation, engineering, and functional application of EVs derived from THP-1 cells, a well-established in vitro model of the human monocyte–macrophage lineage.

The workflow integrates two complementary microfluidic modalities. First, THP-1 cells are exposed to controlled mechanical stress within a high-pressure microfluidic environment, which promotes a reproducible and high-yield release of small EVs. This microfluidic induction strategy offers distinct advantages over spontaneous secretion, including enhanced scalability, reduced processing times, and improved uniformity of the vesicle population.EV preparations were characterized through standard analytical techniques, including nanoparticle tracking analysis, zeta potential measurement, transmission electron microscopy, and immunoblotting for typical vesicle markers. The resulting EVs display characteristic dimensions (~120 nm), intact morphology, and conserved expression of canonical EV markers.

In the second stage, a custom-designed low-pressure microfluidic platform is employed to engineer the isolated EVs with nucleic acid cargo. The gentle hydrodynamic conditions ensure efficient encapsulation while preserving vesicle integrity—a common bottleneck in conventional loading approaches. Notably, the same microfluidic system is also intented to mediate the interaction between engineered EVs and recipient THP-1 cells. This enables a highly controlled exposure environment, supporting the use of EVs as vehicles for cellular transfection while maintaining cell viability and physiological responsiveness.

Across multiple conditions, neither unloaded nor engineered EVs induced cytotoxic effects in undifferentiated or PMA-differentiated THP-1 cells, confirming their biocompatibility and suitability for delivery applications.

Overall, this work highlights the central role of microfluidics in creating an integrated pipeline for EV production, engineering, and downstream applications. The microfluidic framework provides precision, scalability, and reproducibility, addressing key limitations of traditional EV-based methodologies. These findings support the development of next-generation EV platforms for immunotherapy and gene delivery, where microfluidic technologies stand as essential enabling tools.

Biodistribution analysis of targeted and non-targeted nanoparticles in tumor bearing mice using a physiological-based pharmacokinetic model

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 263

Marta Rodriguez-Jimenez [1], Alejandro Serrano-Alcaide [1], Ainara Salgado [1], Sara Zalba [2], Iñaki F Troconiz [1], Maria J Garrido [2]

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Immunomodulation of the tumor microenvironment is a promising cancer treatment strategy. Tumors promote regulatory T cell (Treg) infiltration, characterized by CD25 overexpression, to evade immune responses. While anti-CD25 antibodies deplete Tregs and enhance anti-tumor effect in animal models, this approach causes severe autoimmunity.

Liposomes (LPS) are versatile nanoplatforms capable of improving drug pharmacokinetics and tumor access via the EPR effect. However, this passive tumor delivery is very low (<2% of injected dose); while active targeting, using ligand-conjugated LPS (ILPS), can modestly increase delivery (5-6%). To better understand the complex in vivo distribution of both formulations, a physiological based pharmacokinetic (PBPK) model was proposed to describe longitudinal data across various organs, particularly in tumor.

LPS were formulated by film hydration method, incorporating a fluorescent probe (DiD). Targeted ILPS were prepared by post-insertion method, conjugating anti-CD25 Fab' to DSPE-PEG_{2000}-Maleimide that are incorporated into pre-formed LPS.

Twenty-six C57B6/J mice bearing MC38 tumors (50-80 mm^3 after 7 days) received a single intravenous dose of either saline (control) or 2.3/2 mg lipid for LPS and ILPS, respectively. Biodistribution was assessed over time in plasma, heart, lung, kidney, spleen, thymus, liver, and tumor. Each animal provided a single measurement per matrix. Longitudinal data were analyzed simultaneously using the naïve pool approach with Monolix2024R1.

Despite the inter-animal variability, median data were used to propose a standard PBPK model, which significantly under-predicted the experimental observations, suggesting certain misspecifications. To accurately describe nanoparticles distribution, the model incorporated: (i) the lymphatic system, (ii) tumor accumulation via the EPR effect, and (iii) size-dependent LPS extravasation influenced by organ-specific vascular endothelium. The results show a very low tumor-to-plasma distribution coefficient for both formulations, consistent with limited tumor distribution and delivery. However, the different behavior of ILPs in plasma, tumor and spleen, organs rich in Tregs, suggested an additional receptor-dependent mechanism influencing nanoparticle distribution, currently under further evaluation.

In conclusion the proposed physiological framework is a valuable tool for understanding the complex interaction between these nanoparticles and tumor microenvironment and various organs to improve these current delivery strategies for immunomodulation.

Development and optimization of a stable niosomal nanoformulation of 20-hydroxyecdysone for potential psoriasis therapy

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 256

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Psoriasis is a chronic, inflammatory, autoimmune skin disease significantly impacting quality of life, including psychological and social aspects [1-2]. Despite the availability of various therapies, psoriasis treatment remains challenging; therefore, new and practical therapeutic approaches are being sought, such as the use of compounds with immunomodulatory potential, including 20-hydroxyecdysone (20-HE) [3]. 20-HE exhibits low bioavailability, which can be enhanced by using nanoformulations. Lipid nanocarriers, such as niosomes, are non-toxic and scalable, and can enhance solubility and absorption across biological barriers, and reduce the side effects of substances [4-5]. Niosomes with optimal properties could be effective in treating skin conditions such as psoriasis [6].

This study aimed to develop and optimize niosomal formulations containing surfactants and cholesterol to encapsulate 20-HE, and to evaluate their physicochemical properties, encapsulation efficiency, and stability.

Niosomes were prepared using the thin-film hydration method. The obtained film was hydrated and then subjected to sonication to achieve a homogeneous population of niosomes. Physicochemical parameters, including particle size (SIZE), polydispersity index (PDI), and zeta potential, were measured using dynamic and electrophoretic light scattering techniques. The encapsulation efficiency (EE%) was determined using high-performance liquid chromatography.

The optimized niosomes exhibited a SIZE of 100–300 nm, ideal for topical psoriasis therapy without systemic absorption. The PDI (<0.300) indicated narrow size distribution and formulation homogeneity. Zeta potential values below -30 mV confirmed good stability. The EE% showed significant 20-HE encapsulation within the niosomes. Stability tests at 2-4°C indicated carrier stability.

The 20-HE-loaded niosomes fulfilled the physicochemical and stability criteria for topical delivery systems. These findings highlight their potential as a promising nanocarrier platform for psoriasis therapy, warranting further preclinical evaluation.

Keywords: Psoriasis, 20-hydroxyecdysone, nanotechnology, niosomes

Funding: *Research aimed at developing a new, innovative pharmaceutical form for the topical treatment of psoriasis vulgaris" is being implemented as part of the National Recovery and Resilience Plan, as part of Investment D3.1.1 Comprehensive development of research in medical sciences and health sciences, reference number: 2024/ABM/03/KPO/KPOD.07.07-IW.07-0043/24-00.*

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6. DOI: 10.3390/pharmaceutics17030287

Amphiphilic Copolymer Nanoparticles: Bridging Innovation and Regulation

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 211

Federico Stucchi [1], ***Ilaria Porello*** [1], ***Francesco Cellesi*** [1]

1. *Politecnico di Milano*

Nanomedicine has emerged as a rapidly growing field due to its extensive possibilities in healthcare innovation. Within this context, polymer-based nanomaterials are increasingly explored for advanced diagnostic and therapeutic applications [1]. Although several nanomedicine products have already received regulatory approval from agencies such as the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA), clear guidance specific to polymeric nanosystems remains lacking, underscoring the need for dedicated regulatory standards tailored to nanoscale properties [2].

This work investigates the development of polymeric nanoparticles derived from amphiphilic copolymers with complex architectures as a model system to examine regulatory bottlenecks in the nanomedicine pipeline. Key focus areas include nanoscale characterization and manufacturing challenges that influence clinical translation and regulatory acceptance.

A versatile set of amphiphilic copolymers with different structures and compositions was synthesized using Ring-Opening Polymerization (ROP) and Atom Transfer Radical Polymerization (ATRP) [3,4]. These copolymers were subsequently formulated into nanoparticles by nanoprecipitation and loaded with a reference drug (Figure 1). The resulting formulations establish a baseline for evaluating nanoparticle design, physicochemical characterization, and formulation optimization at the early development stage.

To support future translation to clinical use, standardized and regulatory-aligned workflows need to be implemented to ensure safety, quality, and efficacy across all steps. The insights gained will contribute to strengthening current regulatory frameworks and facilitating the progression of polymeric nanomedicines from laboratory research to patient care.

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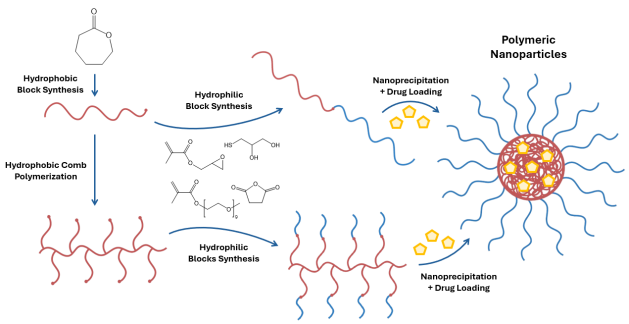

Stucchi abstract - figure 1.png

A scalable microfluidic method for the continuous-flow synthesis and stabilization of hybrid inorganic/organic nanoparticles

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 177

Marco Carofiglio [1], ***Alessandro Masoero*** [1], ***Bianca Dumontel*** [1], ***Alice Balboni*** [1], ***Valentina Cauda*** [1]

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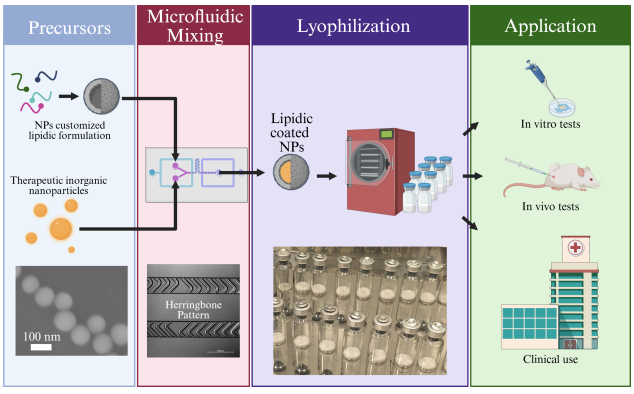
The field of nanomedicine is facing a steep increase in the number of technologies developed by researchers. Inorganic nanoparticles (NPs) often possess powerful therapeutic potentials that are not achievable by conventional small molecules based drugs. However, these inorganic NPs are often unsuitable for direct use in the human body due to their tendency for aggregation and poor biocompatibility. Therefore, they often require surface modification, such as coating with biomimetic shells, including phospholipidic layers.

Despite their potential, the clinical application of these hybrid nanoparticles is hindered by complex synthesis procedures and laboratory-scale production volumes, which inevitably lead to batch-to-batch variability. Moreover, the large-scale production of this kind of nanoconstruct is limited by a very short shelf-life, which often does not exceed a few days.

In this work, we present a general method for developing hybrid inorganic/organic nanoparticles that exploits microfluidic assays to continuously combine the inorganic and organic components. This method can operate in a continuous mode, achieving gram-scale production of lipid-coated nanoparticles in a single working day. Specifically, different types of nanoparticles - ranging from inert silica NPs (as a proof of concept) to biologically active and theranostic ZnO NPs and quantum dots - were coated with a lipidic bilayer whose formulation was adapted to best suit the target nanoparticle core.

The resulting nanoparticles demonstrated superior biocompatibility and hemocompatibility compared to their naked counterparts, confirming performance equivalence with laboratory-scale production methods. Furthermore, the reproducibility of the process is largely improved compared to laboratory-scale production. Finally, we addressed the product's shelf-life by investigating lyophilization, demonstrating that excipients can be added directly during nanoconstruct assembly. This perfectly integrates the lyophilization step into the industrial-scale process.

In conclusion, this work provides the foundation for a true industrial-scale-up for the clinical use of hybrid nanoparticles, allowing nanomedicines to be more reproducible, safer, and, most importantly, feasible for use in a clinical context.



Microfluidic workflow for hybrid nanoparticles fabrication.png

Enhancing phage reliability with solid lipid nanoparticle encapsulation for antimicrobial-resistant infections

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 158

Lorena García Hevia [1]

1. *Insitituto de Investigación en Salud Galicia Sur - CINBIO*

Phage therapy offers a compelling alternative for difficult-to-treat infections in which antimicrobial resistance undermines standard antibiotics. To advance this approach, it is crucial to discover and develop new phages and to formulate them for reliable delivery.

Here we present three newly isolated lytic bacteriophages with strong activity against clinically relevant, drug-resistant bacteria. Each phage displays robust performance on its own, and, critically, their combined use as a cocktail further improves coverage and overall efficacy, consistent with additive or synergistic effects and a lower risk of resistance emergence.

To enhance stability, dosing consistency, and translational reliability, we are encapsulating the cocktail in solid lipid nanoparticles (SLNs). Encapsulation is expected to protect phages during storage and handling, buffer them against environmental stressors, and enable more controlled administration, thereby supporting reproducible therapeutic outcomes.

Together, the discovery of these three complementary phages, their reinforced activity when used in combination, and their SLN encapsulation outline a practical path toward more dependable phage therapy for infections where bacterial resistance is a dominant challenge. Ongoing work focuses on optimizing the SLN formulation parameters and benchmarking performance across relevant strains and models to inform future preclinical development.

A Novel Gold Nanoparticle Carrier for Tyrosine Kinase Inhibitor Delivery

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 98

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Nanotechnologies used in cancer treatment have one of their most important goals set at ensuring effective delivery of the drug to the target site, in optimal concentration and with minimal adverse effects on healthy cells. New nanocarriers are therefore being developed with an emphasis on their beneficial properties, such as biocompatibility, biodegradability, and non-toxicity. Such nanocarriers include chitosan nanoparticles, which have established themselves as suitable drug delivery systems capable of encapsulating a wide range of drugs into their polymer matrix. Chitosan nanoparticles prepared by the ion gelation method are among the most frequently studied polysaccharide-based systems and represent an attractive basis for the development of more sophisticated nanomaterials. In our research, we focused on encapsulating a specific drug from the class of tyrosine kinase inhibitors into the structure of chitosan nanoparticles. We further enriched this system with gold nanoparticles, which are among the most widely used metal nanomaterials in medicine and biology due to their exceptional optical and photothermal properties. The integration of gold nanoparticles into our system significantly influenced its physicochemical characteristics and expanded the possibilities for evaluating parameters such as drug loading, drug release, and interactions in the biological environment of various tumor lines. We confirmed the presence of the encapsulated drug in gold-coated nanoparticles using several analytical methods, including UV/vis spectroscopy, the ATR (Attenuated Total Reflection) method, and Raman spectroscopy. The successful binding of gold nanoparticles to the surface of the chitosan nanocarrier was clearly demonstrated by Transmission Electron Microscopy, which provided a detailed view of the morphology and homogeneous distribution of metal particles. The hybrid system prepared in this way represents a promising approach for use in light-induced therapies, where the photothermal effect of gold nanoparticles could be synergistically applied together with a targeted drug. Our results provide a new perspective on the study of advanced nanomaterials that combine polymer and metal components, while highlighting their potential in the development of effective and targeted anticancer therapy strategies.

Plasmonic Metal Phenolic Network Nanoprobes for Multiplexed Dual-Mode Immunophenotyping

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 44

Lara González Cabaleiro [1], ***Zhixing Lin*** [2], ***Lorena Vázquez Iglesias*** [3], ***Soraia Fernandes*** [4], ***Gustavo Bodelón*** [5], ***Jorge Pérez-Juste*** [1], ***Frank Caruso*** [2], ***Isabel Pastoriza-Santos*** [1]

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Multimodal detection improves accuracy, sensitivity, and reliability by offering mutual validation and minimizing false positives/negatives. In particular, dual-mode surface-enhanced Raman scattering (SERS)-fluorescence shows great analytical potential for biodetection due to their synergistic advantages and built-in cross-validation integrated in a single optical probe. A bimodal SERS-fluorescence nanoprobe consists of a plasmonic nanoparticle functionalized with Raman reporters enclosed within an optically inactive shell.[1] These are typically made of silica, which provides colloidal stability and a supportive scaffold for conjugation with fluorescent entities and biorecognition elements (e.g. antibodies).[2] In this study, we report on the implementation of metal-phenolic networks (MPNs) as coatings for the fabrication of dual-mode SERS-fluorescence nanoprobes based on plasmonic nanoparticles.[3] MPNs adhere to the surface of the metallic nanoparticle thanks to the inherent properties of their phenolic moieties allowing for controlled thickness, while facilitating the seamless conjugation of functional antibodies in a one-step reaction.[4] The plasmonic MPN (PMPN) nanoprobes codified with distinct Raman reporters and fluorescently labelled antibodies allowed the multiplex detection of epidermal growth factor (EGFR) and homing cell adhesion molecule (CD44) receptors in cultured cells by SERS and flow cytometry. This work provides a framework for developing dual-mode SERS-fluorescence nanoprobes based on MPNs that hold great potential for targeted cell imaging and immunophenotyping applications.

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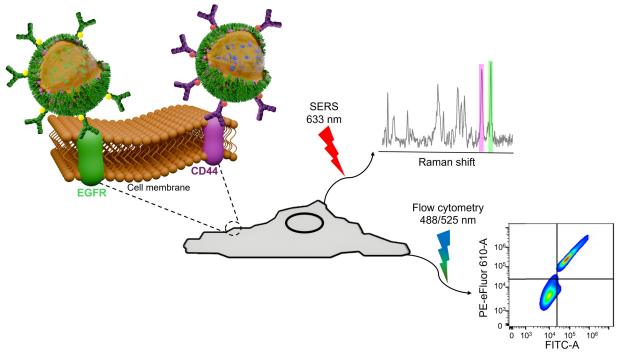


Schematic representation of the multiplex cell targeting. The dual mode probes, conjugated with labeled anti-EGFR and anti-CD44 recognise the EGFR and CD44 expressed in eucaryotic cells. This binding is dual tested by SERS employing a 633 nm laser line where the signal from malachite green (green shadow) and astra blue (pink shadow) are detected, and by flow cytometry employing 488 and 525 nm laser lines, been able to discriminate between HER14 (positive for both biomarkers, right and upper part of the cytogram) and HEK-293 (negative for both, left and lower part of the cytogram) cell lines.

Figure abstract.jpg

Cell-Adhesive Double-Network Self-Healing Hydrogel for Biomedical Applications

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 286

Won-Gun Koh [1], ***JaeWook Park*** [1]

1. *Yonsei University*

This study introduces a novel double-network self-healing hydrogel based on N-carboxyethyl chitosan (CEC) and oxidized dextran (OD), incorporating crosslinked collagen (CEC-OD/COL-GP) to improve its biological and physicochemical properties. The hydrogel, formed through dynamic imine bond formation, demonstrates efficient self-healing within 30 minutes and recovers 92% of its compressive modulus within 2 hours. In addition to its self-healing capabilities, the hydrogel exhibits transparency, injectability, and strong adhesiveness to various substrates and tissues. Biocompatibility studies confirmed its suitability as a cell-culture scaffold, with the collagen network significantly enhancing cell adhesion, spreading, long-term viability, and proliferation. The hydrogel's versatile properties enable the creation of modular assemblies for controlled spatiotemporal drug delivery and co-culture models that mimic angiogenesis in tumor microenvironments. With its potential for constructing complex structures, supporting diverse cell types in 3D environments, and enabling controlled therapeutic delivery, the CEC-OD/COL-GP hydrogel holds great promise for advancements in tissue engineering and medical interventions.

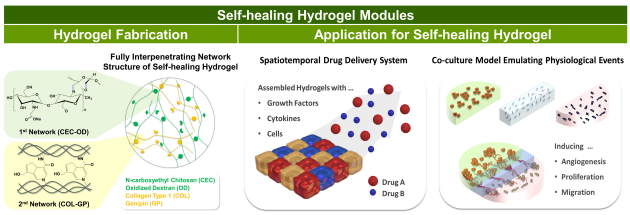


Figure.jpg

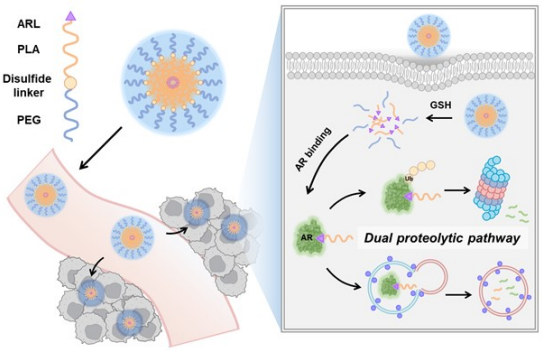
Targeted Protein Degradation in Cancer Therapy via Hydrophobic Polymer-Tagged Nanoparticles

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 289

Won Jong Kim [1], ***Seohee Lee*** [1]

1. *Pohang University of Science and Technology (POSTECH)*

Targeted protein degradation (TPD) strategies offer a significant advantage over traditional small molecule inhibitors by selectively degrading disease-causing proteins. While small molecules can lead to recurrence and resistance due to compensatory pathway activation, TPD addresses this limitation by promoting protein degradation, thereby reducing the likelihood of recurrence and resistance over the long term. Despite these benefits, bifunctional TPD molecules face challenges such as low solubility, poor bioavailability, and limited tumor specificity. In this study, we developed polymer-based nanoparticles that combine TPD strategies with nanotechnology through a hydrophobic tagging method. Hydrophobic polymer-tagged nanoparticles facilitate targeted protein degradation by incorporating hydrophobic polymers that mimic hydrophobic residues in misfolded proteins. This system combines degradation and delivery capabilities within a polymer-based platform, inducing protein degradation while improving solubility, stability, and tumor targeting. These nanoparticles consist of a block copolymer composed of an androgen receptor ligand (ARL)-conjugated hydrophobic polylactic acid (PLA) and a hydrophilic polyethylene glycol (PEG), connected by a GSH-cleavable disulfide bond. In aqueous solutions, this block copolymer (ARL-PLA-SS-PEG) forms micelles that degrade in reducible cellular environments. The micelles demonstrated significant in vitro degradation of the target androgen receptor (AR). Furthermore, they achieved substantial tumor accumulation and significantly inhibited tumor growth in a tumor-bearing mouse model. A mechanistic study revealed that the micelle-mediated TPD occurs *via* a dual pathway involving both proteolysis and autophagosome formation. This approach has the potential to serve as a universal platform for protein degradation, eliminating the need to develop disease-specific TPD molecules.



Scheme1.jpg

Thermal optimization of ivermectin in supercritical carbon dioxide and ethanol to produce nano medicine

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 146

Reem Gahtani [1]

1. *King Khalid University*

The solubility of ivermectin in high pressure carbon dioxide (CO_2) at 338, 328, 318, and 308 K temperatures was investigated with and without an ethanol. Several methods were employed to model the data obtained from the experiments. ivermectin exhibited solubility values ranging from 0.130×10^{-5} to 1.760×10^{-4} in the binary system and 1.880×10^{-5} to 1.237×10^{-4} in the ternary system. The outcome indicated that the addition of ethanol significantly increased the mole fraction of ivermectin in CO_2. The highest impact of ivermectin solubility was found in the ivermectin -Ethanol- CO_2 system at 338 K and 12 MPa, which was about 14.35 times greater than binary system under the same conditions. The models proposed by Jouyban et al. and Sodeifian-Sajadian models showed the best correlation with average absolute relative deviation (AARD%) and Akaike information criterion (AICc) for binary and ternary approaches, respectively. The results confirmed that rapid expansion supercritical solution (RESS) and gas antisolvent (GAS) method can be apply for producing nanoparticles at the suitable ranges of the drug solubility.

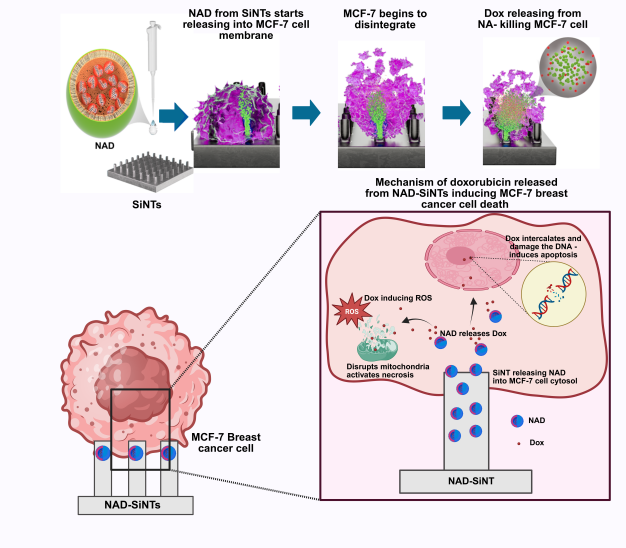
Nanoinjection Platform for Drug Delivery in Breast Cancer Therapeutics

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 122

Kaviya V B [1]

1. *Indian Institute of technology Madras*

Conventional nanomaterial-based drug delivery systems are often limited by rapid burst release, poor cellular uptake, drug degradation, and high local drug concentrations, reducing therapeutic efficacy. To address these challenges, we present a dual strategy integrating (i) doxorubicin encapsulation within thermostable nanoarchaeosomes (NAs), derived from archaeal lipids, and (ii) silicon nanotubes (SiNTs)-based nanoinjection for intracellular delivery. This approach enables efficient transport of nanoarchaeosome-loaded doxorubicin (NAD) into MCF-7 breast cancer cells, inducing membrane perturbation and achieving controlled drug release over 700 hours. NAD–SiNTs exhibit potent cytotoxicity, with an IC_{50} of 60 nM 23-fold lower than free doxorubicin—while maintaining high biocompatibility in NIH-3T3 fibroblasts. Fluorescence-activated cell sorting (FACS) analysis revealed 44% necrosis in MCF-7 cells post-treatment with NAD–SiNTs. Moreover, chick embryo assays and angiogenesis gene expression studies confirm that NAD–SiNTs suppress tumor vasculature genes, effectively inhibiting angiogenesis. These findings position NAD–SiNTs as a promising drug delivery platform, enabling sustained and targeted breast cancer therapy.



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Solubility Enhancement and Anticancer Potential of Piperine–Simvastatin Inclusion Complexes with Methylated β-Cyclodextrin

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 154

Riyad Alzhrani [1]

1. *King Saud University*

Background:

Simvastatin (SIM) and piperine (PIP) possess potent pharmacological and anticancer properties, yet their therapeutic application is limited by poor aqueous solubility and low bioavailability. Cyclodextrin (CD) complexation has emerged as a promising strategy to enhance solubility and stability of poorly soluble drugs.

Aim:

This study aimed to develop and characterize co-loaded inclusion complexes of SIM and PIP using β-cyclodextrin (βCD) and methylated β-cyclodextrin (MβCD) to enhance solubility, bioavailability, and anticancer efficacy against hepatocellular carcinoma (HepG2) cells.

Methodology:

Dual-drug inclusion complexes were prepared by solvent evaporation and microwave irradiation methods at varying drug-to-carrier molar ratios. Phase solubility, saturation solubility, and drug content analyses were performed to determine the optimal formulation. Physicochemical interactions were characterized by Fourier-transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC). In vitro cytotoxicity, apoptosis, and cell cycle analyses were conducted using HepG2 cells to assess the biological activity.

Results:

MβCD-based inclusion complexes demonstrated superior solubilization efficiency compared to βCD, forming stable AL-type complexes with high stability constants (Ks = 527–1037 M^{-1}). The optimized MβCD complex (1:0.5:0.5 ratio, solvent evaporation method) increased solubility up to 1005.9 ± 33.7 µg/mL for PIP and 127.2 ± 4.9 µg/mL for SIM—representing 16- to 44-fold enhancement over pure drugs. FTIR and DSC confirmed successful complex formation and amorphous transformation. The optimized inclusion complex significantly enhanced cytotoxicity against HepG2 cells, inducing over 80% cell death at 50 µM after 48 h. Flow cytometry revealed a two-fold increase in late apoptotic cells and G1 phase arrest, confirming enhanced pro-apoptotic and anti-proliferative activity.

Conclusion:

The co-loaded MβCD inclusion complex markedly improved solubility and anticancer efficacy of PIP and SIM, suggesting a promising oral delivery system for hepatocellular carcinoma therapy.

An Interfacial Effect of Self-Assembled Monolayers on the Performance and Stability of PEDOT:PSS-Based OLED structure

Wednesday, 14th January - 13:30: Poster session (Posters & Coffee Breaks) - Poster - Abstract ID: 326

Sang Geon Park [1], ***Batdelger Ankhnybayar*** [2]

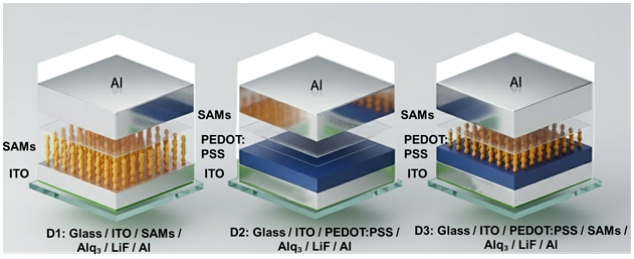
1. *Changwon National University,* ***2.*** *Department of Culture and Technology Convergence, Changwon National University*

In this study, we employ PEDOT:PSS to evaluate the effect of self-assembled monolayers (SAMs) on the hole injection layer (HIL) of organic light-emitting diodes. The device's structure was ITO/PEDOT:PSS/SAMs/NPB/Alq_3/LiF/Al. Various SAMs were coated on PEDOT:PSS to improve surface properties, and their impacts on surface passivation and barrier characteristics were investigated. Fluorinated, silane, or thiol-terminated SAMs were used because they have significant chemical interactions with ITO surfaces. However, the precise mechanisms of interaction between PEDOT:PSS and SAMs are still unknown.

Our findings indicated that adding SAMs to PEDOT:PSS lowered device efficiency by about 0.5-0.8%. Directly applying SAMs to ITO without PEDOT:PSS dramatically increased device performance, reaching a maximum brightness of 8000 Cd/m². These findings indicate that SAMs can successfully passivate ITO surfaces and lengthen device lifetimes, however mixing SAMs with PEDOT:PSS may result in higher surface resistance or undesirable interfacial interactions.

From the standpoint of nanomaterials, SAMs are crucial for managing surface chemistry, charge injection, and interfacial stability, opening up new avenues for OLED interface engineering. The findings are also relevant to biomedical and clinical applications, as OLEDs are increasingly being used in flexible displays, lighting, and optoelectronic medical equipment. The compatibility of SAMs with conductive polymers is critical in these applications, as device stability has a direct impact on operational reliability. Improved surface passivation and interface management in diagnostic OLED sensors can boost sensitivity and measurement precision.

This study emphasizes the relevance of interfacial engineering in OLED device and nanomaterials research by demonstrating how the right selection and integration of SAMs with conductive polymers can have a considerable impact on charge injection, light emission, and device durability. These findings lay the groundwork for the development of flexible, high-efficiency OLEDs with long lifetimes, which could be used in sophisticated optoelectronic devices in consumer electronics and biomedicine.



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Exploiting Dynamicity to Induce Motility: Motion of Membranized Coacervate Motors

Wednesday, 14th January - 14:30: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 171

Loai Abdelmohsen [1]

1. *Eindhoven University of Technology*

Understanding how different building blocks can be assembled into synthetic systems displaying cell-like architectures and functions is a major scientific challenge. Scientists have considered this multidisciplinary challenge as a way to provide insight into the fundamental processes of living systems, concurrently developing diverse potential applications of cell-mimicking constructs. Noteworthy, compartmentalization, or separation of materials from the external environment by a physical boundary (membrane) is a key hallmark for the origin of life – lipid cellular membranes are essential for hosting vital biochemical processes and maintaining the integrity of living cells. Following a bottom-up approach, several synthetic strategies for the creation of artificial compartments at different length scales have been developed, such us the assembly of polymeric vesicles (polymersomes), lipid vesicles (liposomes), virus capsids, colloidosomes, and coacervates. Remarkably, these compartments have been used for the reconstitution of certain cellular functions such as protein expression, metabolite synthesis, enzymatic cycles, transmembrane transport, and motion. Autonomous motion has been an important source of inspiration for scientists who, over the years, have created a variety of synthetic motor systems, imitating biological motility. Notwithstanding, there is a fundamental difference in the way movement is regulated in synthetic and natural systems. Cellular autonomous motion (e.g., vesicular transport and motility), displays adaptive features as a result of random dynamic processes, which are governed by enzyme-mediated energy input and consumption, and molecular interactions. Mimicking dynamic behaviors in synthetic systems has recently drawn much attention from the scientific community. In this presentation I will show how we couple motility of coacervate compartments to a dynamic process, which is maintained by stochastic events and how we compartmentalize such coacervates in giant liposomes and investigate their motion in confinement.

Biomimetic PLGA Nanoparticles Coated with Adipose-Derived Membranes for Targeted Rosiglitazone Delivery in Obesity Therapy

Wednesday, 14th January - 14:46: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 37

Óscar Abelenda Caamaño [1], ***Alba Costa Santos*** [1], ***Mariangel Luna*** [1], ***Marcos Couselo Carreira*** [2], ***Pablo Taboada Antelo*** [1]

1. *Colloids and Polymer Physics Group (GFCP), Department of Particle Physics, Faculty of Physics and Institute of Materials (IMATUS), Campus Vida, Universidade de Santiago de Compostela, 15782 Santiago de Compostela,* ***2.*** *Institute of Health Research (IDIS) of Santiago de Compostela, 15706 Santiago de Compostela*

White adipose tissue (WAT) can be metabolically reprogrammed into energy-dissipating beige adipocytes, a process known as browning, which represents a promising therapeutic strategy against obesity.[1,2] However, systemic administration of browning agents such as rosiglitazone (Rosi) is hindered by off-target effects and limited tissue specificity.[3] To overcome this issue, we developed a targeted nanodelivery platform based on poly(lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) encapsulating Rosi and camouflaged with adipocyte-derived membranes. Rosi was loaded into PLGA NPs with high efficiency (~ 80%), and the nanosystem exhibited pH-responsive release kinetics, best fitted by the Weibull model at pH 5.5 and the Korsmeyer–Peppas model at pH 7.4. Membrane coating, derived from subcutaneous or visceral adipose tissue of lean or obese rats, respectively, was confirmed by FTIR spectroscopy (disappearance of the ester peak at 1750 cm^{-1} and appearance of amide signals), TEM imaging (5–10 nm coating layer), and total protein quantification. The biomimetic NPs demonstrated excellent colloidal stability in physiological-mimicking and cell culture media for at least 7 days, with reduced stability at acidic pH. Notably, they showed no cytotoxicity or pro-inflammatory responses (ROS, IL-6), and exhibited homotypic targeting toward adipocytes. Functional assays revealed significant upregulation of UCP1 expression and browning-associated morphological changes in vitro, including multilocular lipid droplets and reduced cell size. Overall, this membrane-coated nanoplatform offers a safe, efficient, and targeted approach to induce adipose tissue browning, opening new avenues for nanotechnology-driven obesity treatment.

Aknowledgements

We thank to Agencia Estatal de Investigación (AEI) by PID2022-142682OB-I00 and Xunta de Galicia ED431C 2022/18. ERDF funds are also acknowledged.

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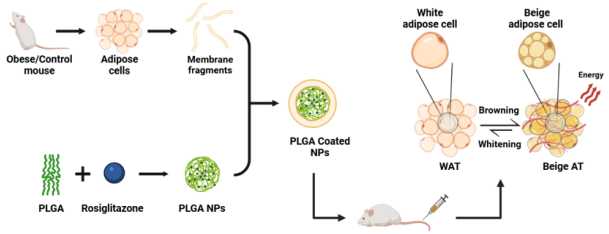

Figure 1: Scheme depicting biomimetic NPs synthesis and therapeutic outcomes. Created with BioRender.

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Targeting the PDAC Microenvironment by Integrating mRNA-LNPs Encoding Mutated Sema3A with a Vascularized Organ-on-Chip Model

Wednesday, 14th January - 15:02: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 19

Giulia Tomaino [1], ***Lucia Salvioni*** [1], ***Metello Innocenti*** [1], ***Luisa Fiandra*** [1], ***Enrico Giraudo*** [2], ***Davide Prosperi*** [1]

1. *University of Milan Bicocca,* ***2.*** *University of Turin*

Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest solid tumors, due to its late diagnosis, poor therapeutic options, and immunosuppressive tumor microenvironment (TME). The TME in PDAC is characterized by an abnormal vasculature, which hampers immune cell infiltration and drug delivery. Semaphorin 3A (Sema3A), has shown promising potential in normalizing tumor vasculature and activating cytotoxic CD8+ T cells, thereby enhancing anti-tumor immunity.

Here, we aim to develop lipid nanoparticles (LNPs) encapsulating the mRNA of a mutated version of Sema3A (mut-Sema3A) and test their impact on PDAC progression. To reduce reliance on in vivo experimentation and develop physiologically relevant platforms that mimics the TME complexity, we established a vascularized PDAC-on-a-chip model using the Organoplate Graft system (Figure 1). This in vitro platform recapitulates key features of the PDAC TME by integrating endothelial cells (EC), tumor spheroids, and immune components within a 3D collagen matrix.

This system provides a controlled environment to study interactions between tumor and various TME cell types offering a powerful in vitro tool to investigate LNP transcytosis and assess the anti-cancer and endothelium-normalizing effects of mut-Sema3A mRNA. Transfection efficiency of mut-Sema3A mRNA and protein secretion have been validated in PDAC and endothelial cell lines. The secreted mut-Sema3A protein has been demonstrated to actively reduce EC migration in Haptotactic EC migration assays.

Preliminary results with LNPs encapsulating Sema3A mRNA proved their ability to transfect both cell lines (Figure 2). The vascularized PDAC-on-a-chip platform will be used to screen and refine mut-Sema3A mRNA-LNPs formulation and delivery protocols. Ultimately, insights gained from this platform will guide the design of in vivo studies in syngeneic orthotopic mouse models of PDAC.

By integrating advanced nanotherapy with a pathologically relevant in vitro model, this project aims to overcome resistance mechanisms in PDAC, offering new opportunities to improve therapeutic outcomes for patients.

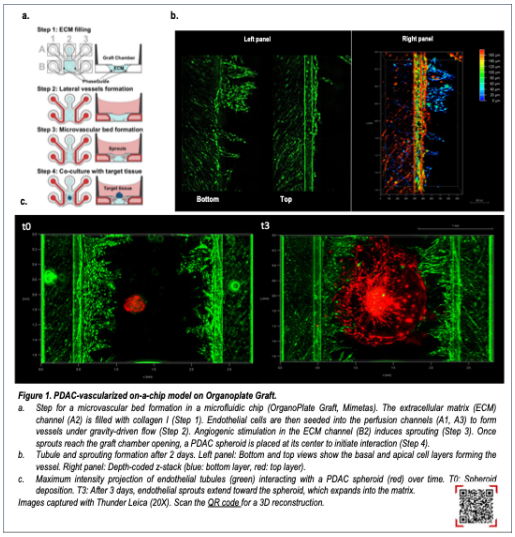


Figure 1. PDAC-vascularized on-a-chip model on Organoplate Graft.

a. Step for a microvascular bed formation in a microfluidic chip (OrganoPlate Graft, Mimetas). The extracellular matrix (ECM) channel (A2) is filled with collagen I (Step 1). Endothelial cells are then seeded into the perfusion channels (A1, A3) to form vessels under gravity-driven flow (Step 2). Angiogenic stimulation in the ECM channel (B2) induces sprouting (Step 3). Once sprouts reach the graft chamber opening, a PDAC spheroid is placed at its center to initiate interaction (Step 4).

b. Tubule and sprouting formation after 2 days. Left panel: Bottom and top views show the basal and apical cell layers forming the vessel. Right panel: Depth-coded z-stack (blue: bottom layer, red: top layer).

c. Maximum intensity projection of endothelial tubules (green) interacting with a PDAC spheroid (red) over time. T0: Spheroid deposition. T3: After 3 days, endothelial sprouts extend toward the spheroid, which expands into the matrix.

Images captured with Thunder Leica (20X). Scan the QR code for a 3D reconstruction.

Figure1. pdac-vascularized on-a-chip model on organoplate graft.png

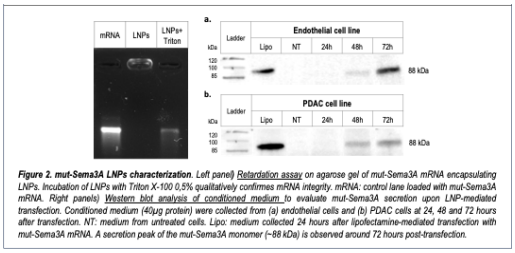


Figure 2. mut-Sema3A LNPs characterization. *Left panel) Retardation assay on agarose gel of mut-Sema3A mRNA encapsulating LNPs. Incubation of LNPs with Triton X-100 0,5% qualitatively confirmes mRNA integrity. mRNA: control lane loaded with mut-Sema3A mRNA. Right panels) Western blot analysis of conditioned medium to evaluate mut-Sema3A secretion upon LNP-mediated transfection. Conditioned medium (40µg protein) were collected from (a) endothelial cells and (b) PDAC cells at 24, 48 and 72 hours after transfection. NT: medium from untreated cells. Lipo: medium collected 24 hours after lipofectamine-mediated transfection with mut-Sema3A mRNA. A secretion peak of the mut-Sema3A monomer (~88 kDa) is observed around 72 hours post-transfection.*

Figure2. mut-sema3a lnps characterization.png

Micro-physiological systems for controllable drug delivery to the brain

Wednesday, 14th January - 15:18: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 16

Giulia Silvani [1], ***Evelyn Szabo*** [1], ***Nicolas Warburton*** [1], ***Zeyan Xu*** [1], ***Martina Stenzel*** [1], ***Kristopher A. Kilian*** [1]

1. *University of New South Wales*

INTRODUCTION

Efficient drug delivery to the brain remains a major obstacle in treating glioblastoma (GBM), largely due to the protective function of the blood–brain barrier (BBB) and the tumor's ability to resist therapy through microenvironment-driven plasticity. Traditional *in-vitro* models lack physiological relevance, failing to recapitulate the dynamic interactions between tumor and vasculature, thereby limiting the ability to accurately assess therapeutic response and ultimately slowing the development of effective treatments.

METHODS

We engineered a micro-physiological system with perfusable blood vessels under flow and a tumor compartment with brain-mimetic ECM, replicating key structural and transport features of the GBM tumor microenvironment (Figure 1A). The platform was validated using fluorescent tracers to confirm BBB integrity (Figure 1B) and soluble glycopolymer to assess flow-driven transport. Temozolomide (TMZ), the clinical standard-of-care, was then delivered in both free and nanoparticle forms and hydrogel stiffness was modulated to mimic different tumor microenvironment conditions, providing a controlled framework to explore how mechanical features of the ECM contribute to therapy resistance and drug penetration.

RESULTS AND DISCUSSION

Fluorescent tracers confirmed barrier function in tumor-free conditions, while GBM spheroids disrupted the vasculature, replicating the leaky vessel phenotype observed in patients (Figure 1C). Under dynamic flow conditions, variations in glycopolymer architecture (Figure 1D) led to differential tumor accumulation (Figure 1E), which remained undetected in conventional static assays (Figure 1F). TMZ-loaded nanoparticles (Figure 1G) demonstrated improved tumor penetration and reduced GBM invasiveness compared to free TMZ, supporting enhanced distribution and functional efficacy within the tumor microenvironment (Figure 1H). Notably, GBM spheroids embedded in softer matrices displayed increased resistance to treatment and adopted an amoeboid morphology, suggesting an adaptive invasive phenotype.

CONCLUSION

Our GBM-on-chip platform replicates key features of the tumor–vasculature interface and enables real-time analysis of drug delivery, therapeutic response, and microenvironment-driven resistance. By offering detailed mechanistic insight into tumor adaptation and transport dynamics, this scalable, ethical, and human-relevant system provides a predictive alternative to animal models and a powerful tool for the preclinical development of brain-targeted therapies.

ACKNOWLEDGEMENTS

This work was supported by Charlie Teo Foundation, Research Rebel Awards program and UNSW's 3Rs grant scheme.

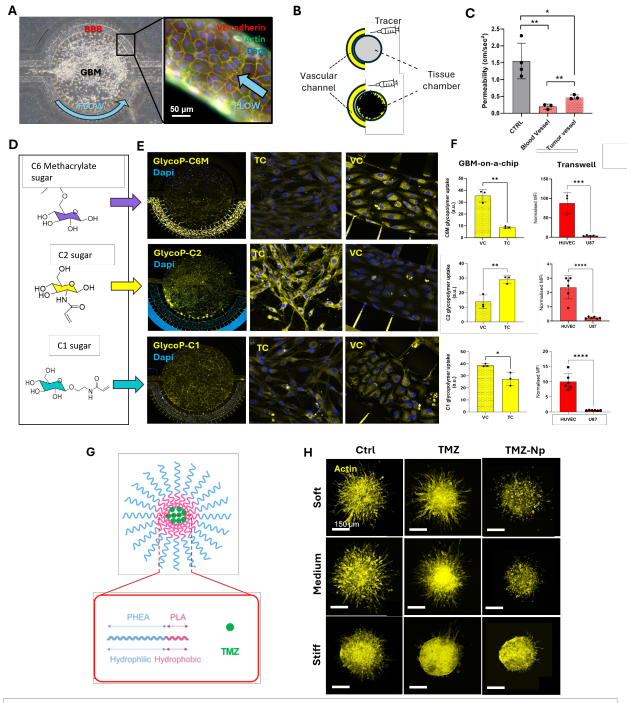


Figure 1. Microfluidic GBM-on-chip (A) recapitulates vascular disruption (B,C) and distinguishes glycopolymer uptake under flow (D-F). TMZ-loaded nanoparticles (G) enhance tumor penetration and suppress GBM invasiveness, supporting improved therapeutic efficacy (H).

Figure 1.png

TRANSDERMAL PATCH TECHNOLOGY BASED ON NANOFIBERS FOR DRUG DELIVERY

Wednesday, 14th January - 15:34: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 6

Jose M. Lagaron [1], ***Jorge Teno*** [2], ***Cristina Prieto*** [1], ***Zoran Evtoski*** [1], ***Ana Kramar*** [1]

1. *IATA-CSIC,* ***2.*** *Bionanopharma SL*

This presentation details the development of a multilayer patch platform created through electrospinning, utilizing polymeric biomaterials aimed at enhancing transdermal drug delivery. Polyethylene oxide served as the matrix material in combination with various permeability enhancers to optimise the release properties and permeation kinetics of a drug model compound, caffeine. The electrospun multilayer patches were characterized using scanning electron microscopy (SEM), attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR), and wide-angle X-ray scattering (WAXS). Drug permeation kinetics were analyzed and modeled using Franz diffusion cells. Initially, penetration was evaluated with a multilayer artificial membrane, and the most effective candidate was subsequently tested with human biopsy skin, revealing significant similarities in the amount permeated, though differing kinetic profiles.

Rational Design of bio-inspired nanoparticles for cancer treatment as on-demand triggerable nanotheranostics

Wednesday, 14th January - 14:30: Prevention and Treatment of Diseases (Room 1) - Oral - Abstract ID: 180

Valentina Cauda [1]

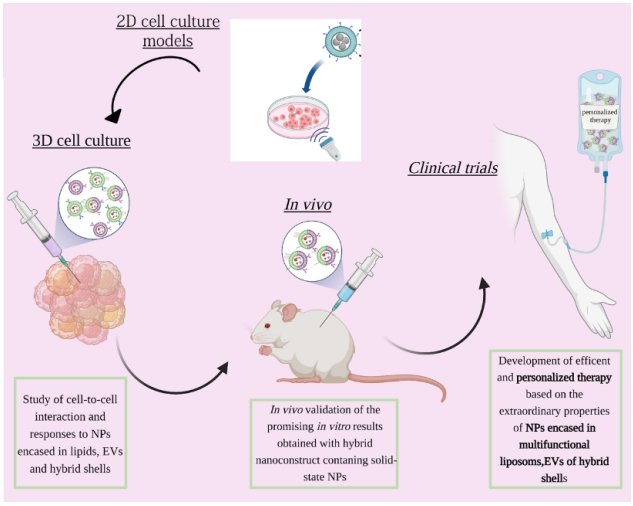
1. *Department of Applied Science and Technology, Politecnico Di Torino*

Cancer remains a major global health challenge, heavily requiring the development of multifunctional theranostic systems that combine precision targeting, robust therapeutic efficacy and diagnosis in a single platform. Here, we describe the preparation of a biomimicking, biocompatible and stimuli-responsive nanoparticle aiming at impairing tumor growth and proliferation.

We developed iron-doped zinc oxide nanocrystals via a wet-chemical method, designed to leverage both diagnostic and therapeutic capabilities. Iron doping imparts biocompatible properties, while the semiconductor nature of ZnO enables the generation of reactive oxygen species (ROS) under external stimulation by acoustic pressure waves, like ultrasound or shock waves, as therapeutic mode of action. Furthermore, these nanocrystals show to greatly reduce the cavitation threshold of ultrasound, allowing to explore also imaging functions. To enhance stability and selectivity, we developed lipidic coatings either inspired to COVID-19 vaccines or biomimicking natural extracellular vesicles. These lipid bilayers include, among others, a functional lipid covalently linked to a targeting peptide or fragmented monoclonal antibodies. These targeting moieties significantly increase nanoparticle uptake by malignant cells both in solid and hematological tumors.

The nanoparticles were tested on different tumor models, from hematological cancers, like B-cell and T-cells lymphomas, multiple myelomas, and solid tumors (pancreatic, colorectal, and osteosarcoma ones), starting from two-dimensional (2D) monolayers to physiologically relevant three-dimensional (3D) spheroid models, up to more complex 3D geometries and in vivo mice models, until patients' derived cells. While the 2D cultures offer initial insight into the safe-by-design properties of the NPs, the 3D models provide a more accurate mimic of in vivo conditions and are particularly important for ultrasound-based treatments, where wave propagation in 3D influences therapeutic outcomes. In the in vivo setting, the therapeutic and imaging effects were most pronounced in the group receiving NPs with ultrasound stimulation. This combination resulted in a marked decrease in tumor volume, increased immune cell infiltration, enhanced tumor cell apoptosis, extended survival of treated mice, and high contrast signal visualizing the tumor mass.

By combining triggered therapy with targeted delivery and imaging capabilities, this nanoplatform represents a promising step forward in the pursuit of more flexible and potent strategies against treatment-resistant malignancies.



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Nanoparticle core guides the choice of cell membrane coating method

Wednesday, 14th January - 14:46: Prevention and Treatment of Diseases (Room 1) - Oral - Abstract ID: 145

MOATAZ ZEWAIL [1]

1. *University of Adelaide*

Cell membrane-coated nanoparticles (NPs) have emerged as a promising platform for drug delivery, offering enhanced cellular uptake and improved therapeutic efficacy. Among the methods used to fuse cell membranes with NP cores, extrusion and sonication are the most widely employed. However, a clear guide for selecting between these two techniques based on NP type remains lacking, leading to inefficiencies in therapeutic outcomes and the need for extensive experimental optimization. In this study, we explored the influence of material type and drug loading on the fusion of cancer cell membranes (4T1) with NP cores using extrusion and sonication. Lipid nanoparticles and polymeric nanoparticles with varying drug-loading levels, along with silica nanocapsules with different mechanical stiffness, were used as core materials to investigate cell membrane coating efficiency. Our results indicate that increasing drug loading enhances mechanical stiffness and alters surface hydrophobicity. The interplay between NP stiffness and surface hydrophobicity is crucial in determining the appropriate cell membrane coating method. Extrusion is better suited for coating softer, more hydrophobic NPs, while sonication is preferable for NPs with lower hydrophobicity and greater mechanical stiffness. The efficiency of cell membrane coating was assessed based on stability, coating degree, and biological performance. These findings provide critical insights into selecting the appropriate cell membrane coating method to optimize therapeutic outcomes, advancing the potential of cell membrane-coated NPs in drug delivery applications.

Multifunctionalization of Iron Oxide Nanocubes for the Treatment of Metastatic Melanoma

Wednesday, 14th January - 15:02: Prevention and Treatment of Diseases (Room 1) - Oral - Abstract ID: 116

Erica Frostegård [1]***, Cecilia Menard-Moyon*** [1]

1. *CNRS, Immunology, Immunopathology and Therapeutic Chemistry, UPR 3572, University of Strasbourg, ISIS, 67000 Strasbourg*

Chimeric antigen receptor (CAR)-T cell therapy has revolutionized the treatment of several hematological malignancies. However, their application in solid tumors is limited by 1) poor infiltration due to the physical structure of solid tumors, and 2) low activity and proliferation caused by the immunosuppressive tumor microenvironment.[1] We aim to overcome these barriers by developing nanoparticles that can generate heat under both alternating magnetic field and laser irradiation, generate reactive oxygen species (ROS), and deliver therapeutic molecules to remodel the tumor microenvironment and favor the infiltration and proliferation of CAR-T cells. In this regard, we synthesized iron oxide nanocubes with an average size of 23 nm (Figure 1a) using a hydrothermal method previously reported.[2] They were first transferred to water via a ligand exchange with citric acid (CA). To enhance their photothermal properties and facilitate the conjugation of therapeutic molecules, they were coated with a thin polydopamine (PDA) layer. The NPs exhibited heating both under laser irradiation and alternating magnetic field (Figure 1b,c). The PDA was doped with copper ions for the generation of ROS to potentially induce cuproptosis.[3] To track the NPs in vivo, a NIR-emitting fluorophore was conjugated to the PDA by amidation. A peptide that binds to the vascular endothelial growth factor (VEGF) receptor was conjugated by Michael addition with the aim to target the tumor and hinder metastasis due to the antiangiogenic effect of the VEGF receptor blocking.[4] The NPs had a slightly larger hydrodynamic size and a positive zeta potential after the peptide conjugation (Figure 1d,f). Biological experiments will be performed soon to assess the NP targeting capability and their therapeutic efficiency.

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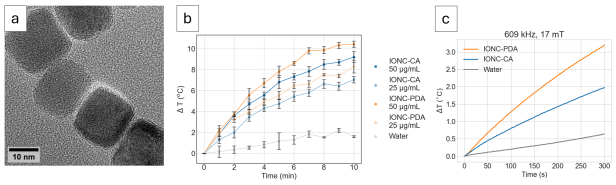

Figure 1a) High-resolution transmission electron microscopy image of IONCs. b) Temperature increase of IONC-CA and IONC-PDA under laser irradiation (808 nm, 0.5 W/cm^2). c) Temperature increase under an alternating magnetic field (609 kHz, 17 mT, 0.4 mg Fe/mL).

Fig abstract.png

Loco-regional treatment with temozolomide-loaded thermogels against glioblastoma

Wednesday, 14th January - 15:18: Prevention and Treatment of Diseases (Room 1) - Oral - Abstract ID: 79

Mauro Comes Franchini [1], ***Erica Locatelli*** [1]

1. *Department Of Industrial Chemistry "Toso Montanari*

Glioblastoma multiforme (GBM) is the most aggressive primary tumor of the central nervous system, with a poor prognosis due to its location behind the blood–brain barrier (BBB). Temozolomide (TMZ) remains the first-line treatment, but its limited BBB penetration requires high systemic doses, resulting in significant side effects and reduced therapeutic benefit.

To address these limitations, we developed new injectable hydrogel systems for local drug delivery directly at the tumor site. Specifically, a chitosan–β-glycerophosphate thermogel (THG) was combined with mesoporous silica nanoparticles (SiO_2) or polycaprolactone microparticles (PCL) to enhance loading and sustained release of TMZ. The biocompatibility of THG–SiO_2 and THG–PCL was confirmed by in vitro cell viability and in vivo histological analyses. When loaded with TMZ, both formulations induced tumor cell death in vitro and significantly reduced recurrence in an orthotopic human glioblastoma mouse model compared to untreated controls.

In parallel, we explored nanocellulose-based hydrogels for localized drug delivery. Nanocellulose offers excellent biocompatibility, tunable porosity but often suffers from uncontrolled burst release. We synthesized a novel bifunctional crystalline nanocellulose (CNC), and hydrogels were prepared using polyamines, enabling electrostatic or covalent crosslinking. As a proof-of-concept, doxorubicin was incorporated into these CNC-based gels, demonstrating sustained release over three weeks without an initial burst effect.

Together, these results highlight the promise of integrating biocompatible hydrogels—whether based on THG with SiO_2 or PCL carriers for TMZ, or on bifunctional CNC for prolonged delivery of other chemotherapeutics—as effective local treatments for aggressive tumors like GBM.

These innovative injectable systems aim to bypass the BBB, maximize local drug concentration, and reduce systemic toxicity, opening new avenues for safer and more effective brain cancer therapies.

Funding: We acknowledge financial support under the National Recovery and Resilience Plan (NRRP), Mission 6, Component 2, Investment 2.1, published on 24.04.2023 by the Italian Ministry of Health (PNRR-TR1-2023-12377370), funded by the European Union - NextGenerationEU - Project Title: Locoregional administration of therapeutic hydrogels to overcome the blood-brain barrier and prevent glioblastoma recurrences, CUP F13C23003200006 (Unit 1), CUP B53C23008320006 (Unit 2), CUP J33C23004200006 (Unit 3), CUP B63C23001870006 (Unit 4).

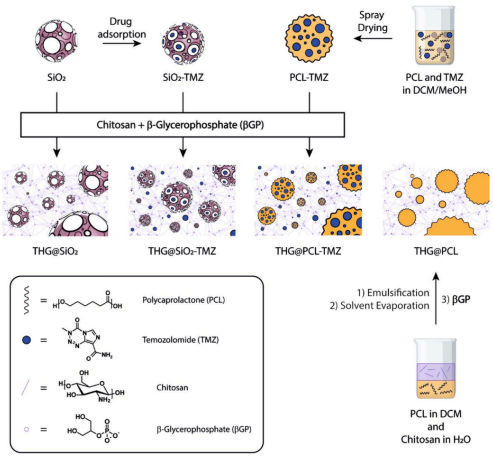

Fig-1.png

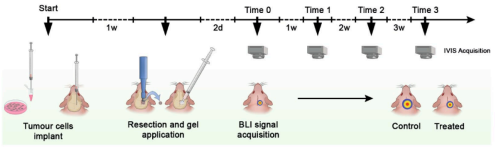

Fig-2.png

Engineering Plasmonic Nanoparticle-Bacteria Biohybrids for Cancer Therapy and Biosensing

Wednesday, 14th January - 15:34: Prevention and Treatment of Diseases (Room 1) - Oral - Abstract ID: 35

Lorena Vázquez-Iglesias [1], ***Lara González-Cabaleiro*** [2], ***Carlos Renero-Lecuna*** [1], ***Luis Liz-Marzan*** [3], ***Jorge Pérez-Juste*** [2], ***Isabel Pastoriza-Santos*** [2], ***Gustavo Bodelón*** [4]

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Bacterial cells have emerged as powerful tools in cancer therapy due to their innate tumour-targeting abilities, high motility, immunogenicity, and capacity for controlled therapeutic delivery[1]. Integrating these living systems with inorganic materials has led to the creation of functional biohybrids—innovative constructs at the intersection of biology and materials science. Among these, plasmonic nanoparticles are particularly promising for applications in nanomedicine, including drug delivery, photothermal and magnetothermal therapies, photodynamic therapy, and imaging via surface-enhanced Raman scattering (SERS)[2].

This study focuses on engineering robust protein-protein interactions to enable the precise assembly of nanoparticles on bacterial surfaces, forming a flexible and efficient anticancer platform. We report the successful development of bacterial-nanoparticle hybrids using the SpyTag/SpyCatcher covalent system. These live biohybrid microrobots, which combine genetically engineered *Escherichia coli* with plasmonic nanoparticles, offer a novel approach to cancer treatment. For this purpose, gold nanorods (AuNRs) and nanocapsules functionalized with SpyCatcher were assembled onto *E. coli* cells expressing SpyTag via the intimin display system[3]. The resulting biohybrids, bearing synthetic adhesins targeting the epidermal growth factor receptor (EGFR), were evaluated in vitro for their targeting and imaging capabilities using SERS. To assess the therapeutic efficacy of AuNRs, photothermal therapy (PTT) was performed using a 1064 nm laser

In vitro assays confirmed the successful functionalization of nanoparticles and the specific binding of NP-SpyCatcher-*E. coli* biohybrids to EGFR-expressing cells. The biohybrids exhibited dual-mode functionality, enabling both high-resolution molecular imaging via surface-enhanced Raman scattering (SERS) and localized photothermal ablation through photothermal therapy (PTT). These results highlight the potential of engineered bacterial biohybrids as multifunctional theranostic agents for precision oncology applications.

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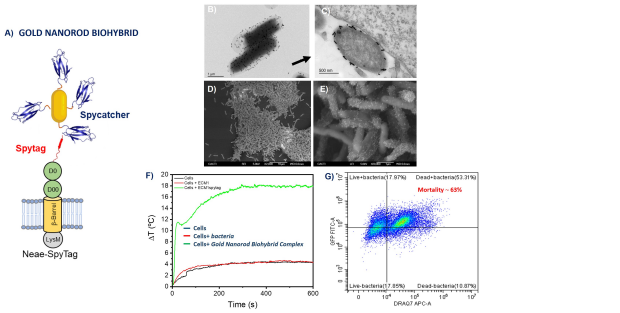

Figure 1: Analysis of Gold Nanorod Biohybrid. A) Gold Nanorod Biohybrid complex structure. B) TEM image of Gold Nanorod complex. C) TEM images of cell- bound Gold Nanorod complex expressing EGFR. D,E) SEM images of cell- bound Gold Nanorod complex expressing EGFR. F) Transient temperature of living cells incubated with bacteria or bacteria-AuNRs biohybrids during hyperthermia treatment (1060nm). G) Flow cytometry data of DRAQ7-labeled cells (indicative of apoptosis) after 10 min of hyperthermia treatment (1060nm).

Figure 1.jpg

Hydrophilic Polymer Brushes as Key Determinants of Protein Corona Resistance in Polymersomes

Wednesday, 14th January - 16:20: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 265

Valentino Barbieri [1], ***Subhadip Ghosh*** [1], ***Laura Rodríguez Arco*** [2], ***Vanina Cosenza*** [1], ***Lorena Ruíz Perez*** [1], ***Giuseppe Battaglia*** [1]

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When exposed to biological fluids, nanoparticles are rapidly coated by a dynamic layer of adsorbed biomolecules known as the protein corona. This layer redefines their physicochemical identity, influencing circulation time, biodistribution, and cellular uptake.[1] Controlling protein corona formation is therefore crucial not only to prevent opsonization and premature clearance by the immune system,[2] but also to preserve the integrity of engineered functionalities such as multivalent ligand display and targeted binding. Inconsistent or uncontrolled corona formation can mask recognition motifs, alter surface charge, and lead to unpredictable therapeutic outcomes, thus posing a major obstacle to the rational design and reproducibility of nanomedicines.[3]

In this work, we investigate the role of hydrophilic polymer brushes in modulating protein adsorption on polymersomes, i.e., self-assembled vesicular nanostructures formed from amphiphilic block copolymers. By combining single-molecule and ensemble-average techniques, we analyze the nano–bio interface across different scales. Fluorescence correlation and cross-correlation spectroscopy offer insights into mutual interactions between proteins and polymersomes at the single-molecule level, while chromatographic and light-scattering analyses quantify protein binding and assess colloidal stability in bulk. We deploy this experimental protocol to explore and compare the performances of the most commonly chosen hydrophilic brush chemistries in nanomedicine.

Our results confirm that neutral, densely packed hydrophilic polymer brushes generate effective steric and hydration barriers that inhibit both hard and soft corona formation, even in complex serum environments. This resistance, however, varies across different polymer chemistries, confirming that interfacial water structuring and polymer chain conformation play key roles in determining the extent and time scales of nonspecific interactions. Together, these findings provide insight into how nanoscale surface chemistry dictates biofouling behavior and highlight practical design principles for engineering next-generation stealth nanodrugs capable of precise, reproducible, and long-circulating therapeutic effect.

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Immune-enriched human lung organoids as a platform for nanotoxicity evaluations

Wednesday, 14th January - 16:36: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 189

Sandra Vranic [1]

1. *Nano-Cell Biology Lab, Centre for Nanotechnology in Medicine, University of Manchester*

Advances in in-vitro culture systems have stimulated an interest in more reliable testing approaches that predict nanomaterial toxicity risks and align with the 3Rs framework. Lung organoids are one example, and display functions consistent with their in-vivo counterparts. We have previously established a human embryonic stem cell-derived lung organoid exposure model that utilises microinjection to deliver nanomaterials into the airspace-like lumen of organoids (1). These organoids exhibit the six major proximal (goblet, basal, club, ciliated) and distal (AECI/II) epithelial cell types of the adult lung and contain functional cells, evidenced by active ciliary beating and surfactant/mucin deposition.

Here, we advanced the lung organoid model complexity by incorporating a functional immune component – human embryonic stem cell-derived macrophages and assessed its suitability as a tool for nanoplastics toxicity assessment. We evaluated the pulmonary toxicity of nanometric polystyrene nanospheres (PS, 50-500nm) and Poly-Ethylene-Terephthalate fragments (PET, 50-200nm) from plastic bottles. Lung organoids, with and without a macrophage component, were exposed with PS or PET for up to 7 days. Using flow cytometry, lung epithelial cells showed an increased PET uptake compared to PS, with no significant impact on organoid viability. Histological analysis revealed distinct areas in which the nanoplastics localise, and their interaction with airway cells and macrophages. Importantly, macrophages were found to capture PS/PET leading to reduced mucus production and alleviated DNA damage, which were all found in the lung organoids exposed to PS/PET in the absence of macrophages.

With further validation, our lung organoid-macrophage model may not only reduce the need for rodent inhalation studies, but also replace the current use of simple in vitro pulmonary models for toxicology studies.

1. Issa et al., Nano Today, 2024, 56, 102254

Graphene flakes as versatile carriers for lysosomal enzymes: activity, delivery kinetics, and bio-persistence in patient-derived fibroblasts

Wednesday, 14th January - 16:52: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 188

Sandra Vranic [1]

1. *Nano-Cell Biology Lab, Centre for Nanotechnology in Medicine, University of Manchester*

Lysosomal storage disorders (LSDs) are a group of metabolic diseases affecting 1 in 4,000-6,000 births. In this pathology, cells are unable to degrade specific substrates in the lysosomes due to the absence/enzyme deficiency, causing progressive and irreversible damage to multiple organs and body systems. There is no cure for LSDs, however standard therapy is intravenous administration of the missing/deficient enzyme, known as enzyme replacement therapy (ERT).

One of the main barriers to effective ERT is insufficient delivery of enzymes to target cells and lysosomes. We previously reported that biocompatible graphene flakes (GFs) can act as efficient carriers for lysosomal enzymes in Mucopolysaccharidosis (MPS) VI fibroblasts, reducing the enzyme dose required to achieve substrate degradation (1). In the present work, we broadened the scope of GF-based delivery by: (i) expanding investigations to Fabry's and Pompe's patient-derived fibroblasts, (ii) assessing the kinetics of substrate degradation over time, and (iii) examining the bio-persistence of GFs within patient-derived cells.

GFs (75 µg/mL) successfully complexed commercially available enzymes for Fabry's and Pompe's disease, as demonstrated by changes in hydrodynamic size and zeta potential, as well as excellent aqueous dispersibility across a range of concentrations. Enzyme activity assays confirmed that >80% of enzymatic activity was retained following complexation, underscoring the versatility of GFs as delivery platform. To address long-term safety, we monitored GF persistence in MPS VI fibroblasts up to 21 days post-exposure using complementary techniques (optical and confocal microscopy, flow cytometry, UV/visible and Raman spectroscopy). A progressive reduction in intracellular granularity was observed, accompanied by redistribution of GFs from perinuclear to cytosolic regions, consistent with exocytosis. By day 21 post treatment, <20% of treated cells retained detectable GFs. These findings demonstrate that graphene flakes are versatile carriers capable of delivering active lysosomal enzymes across multiple lysosomal storage disorders, while also being gradually eliminated from cells. This positions GFs as a promising platform to enhance both the efficacy and safety profile of future ERT strategies.

1. Chen et al., Nanoscale, 2023, 15, 9348-9364.

Effect of Liposome Rigidity on Corona Formation and Its Implications for Uptake by Cell

Wednesday, 14th January - 17:08: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 58

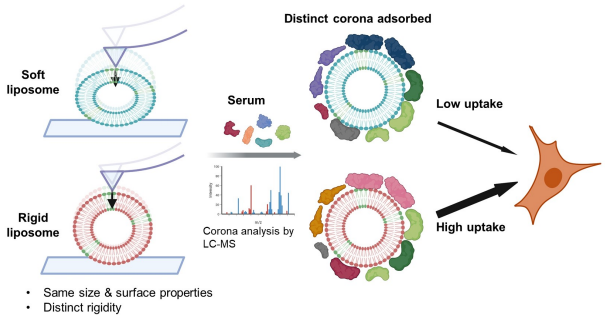
Xinyu Ma [1], ***Feng Zhao*** [1], ***Sander de Weerd*** [1], ***Ilaria Squillante*** [2], ***Giuseppe Portale*** [2], ***Wouter H. Roos*** [2], ***Anna Salvati*** [1]

1. *Nanomedicine and drug targeting department, Groningen Research Institute of Pharmacy,University of Groningen,* ***2.*** *University of Groningen*

Nano-sized materials have been extensively investigated for their potential application in delivering cancer therapeutics. Numerous studies are trying to elucidate how nanoparticle properties, such as size, charge, material etc., affect nanoparticle behavior in organisms and at the cellular level. Among these properties, nanoparticle rigidity, the ability of the object to resist deformation upon an applied force, is emerging as one of the key physicochemical property of nanomaterials influencing their cellular uptake and in vivo behavior. However, the mechanisms behind the observed differences are still largely unknown. In particular, while it is known that the interaction of nanomaterials with biological fluids and the resulting adsorption of a corona on their surface strongly controls the subsequent behavior at the cell and organism level, much less is known on whether nanoparticles of different rigidity adsorb different coronas.

To address this question, we used lipids with identical head groups but differing alkyl chains to prepare liposomes with same surface properties and size, but distinct rigidity. The liposomes and their transition temperature were characterized and atomic force microscopy imaging confirmed the very different mechanical properties. Cellular uptake studies demonstrated that rigid liposomes exhibited higher internalization than the soft ones, and endocytic inhibition experiments revealed distinct mechanisms were involved in the uptake of the two liposomes. Importantly, proteomic analysis showed that rigid and soft liposomes did adsorb very different coronas, hence nanoparticle mechanical properties affect corona formation and composition. As a next step, RNA interference and competition studies were used to test and compare the role of different receptors in the uptake of the two liposomes. The results indicated that the enhanced uptake of rigid liposome could be explained by the observed differences in the adsorbed corona molecules and the different uptake efficiency is not solely due to the different mechanical properties, but results from the effect of liposome mechanical properties on corona formation.

Taken together, our study provides a mechanistic explanation for the impact of nanoparticle rigidity on biological interaction and shows that nanoparticle mechanical properties indirectly shape cellular uptake by affecting the composition of the adsorbed protein corona upon contact with biological fluids.



Graphic abstract.jpg

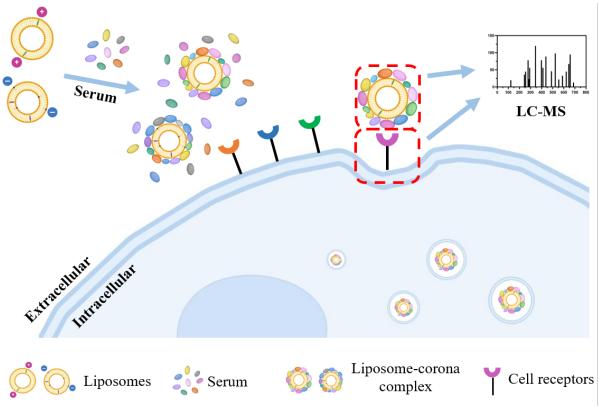
Why do positive nanoparticles usually have higher uptake than negative ones? Comparing protein corona and cell receptors

Wednesday, 14th January - 17:24: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 57

Feng Zhao [1], ***Diksha Nayyar*** [1], ***Young Soo Hwang*** [1], ***Roberta Bartucci*** [1], ***Anna Salvati*** [1]

1. *Nanomedicine and drug targeting department, Groningen Research Institute of Pharmacy,University of Groningen*

Positively charged nanocarriers usually show higher uptake than neutral or negatively charged ones, which is commonly attributed to electrostatic interactions with negatively charged cellular membranes. However, in biological environments, nanoparticle surfaces are masked by biomolecule corona and become neutral. This raises the question of whether charge alone explains uptake differences. To this end, by preparing a series of liposomes with increasing concentration of positively charged lipids, we explored how the amount of positive charges affects liposome stability, toxicity and uptake efficiency. While a higher positive charge enhanced uptake, it also caused aggregation in serum and increased cytotoxicity. With the lower amount of positively charged lipid, a stable liposome could be obtained, without evident toxicity on cell functions. Compared to a negative liposome with equal charge density, the optimized positive liposome demonstrated higher uptake. To explore the underlying mechanisms, different proteomics-based approaches were combined to characterize the protein coronas adsorbed on the liposome surfaces, and the cell surface proteins involved in their internalization. Protein coronas were isolated via size exclusion chromatography and characterized by mass spectrometry and the internalized cell surface proteins were isolated using a reversible biotin-based cell surface biotinylation method. Next, we combined competition and adhesion studies with RNA interference and characterized the mechanisms of endocytosis to dissect the role of individual receptors and corona proteins in the uptake of the two liposomes. We demonstrate that despite the different charge, the uptake of both liposomes is mediated by the interaction with negatively charged cell surface proteoglycans [4]. Additionally, despite the different uptake efficiency, comparable mechanisms of uptake are involved in their internalization. However, the different coronas adsorbed on the two liposomes led to different adhesion to the cell membrane and interaction with different receptors. These results show that the higher uptake of positively charged liposomes cannot be simply attributed to electrostatic interactions with the cell membrane, but rather to differences in the protein corona composition and cell surface receptors involved in their internalization.



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Next-generation targeted protein nanoparticles for precision drug delivery to the tumor microenvironment

Wednesday, 14th January - 17:40: Novel Delivery Strategies (Auditorium) - Oral - Abstract ID: 78

Eric Voltà Durán [1], ***Lorena Alba Castellon*** [2], ***Isolda Casanova*** [2], ***Hector Lopez-Laguna*** [3], ***Alberto Gallardo*** [2], ***Antonio Villaverde*** [4], ***Ugutz Unzueta*** [5], ***Esther Vazquez*** [4], ***Ramon Mangues*** [2]

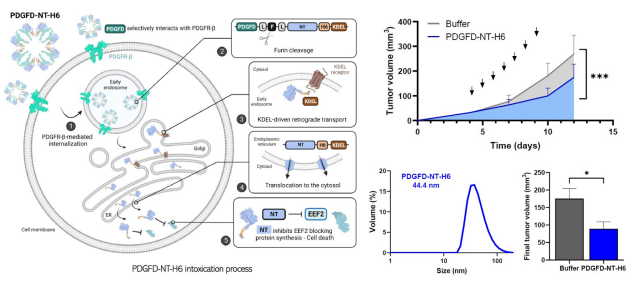
1. *Universitat Politècnica de Catalunya,* ***2.*** *Institut de Recerca Sant Pau (IR Sant Pau),* ***3.*** *Universitat Internacional de Catalunya,* ***4.*** *Universitat Autonoma de Barcelona,* ***5.*** *Institut de Recerca Sant Pau*

Precision delivery of therapeutic proteins remains a major challenge in oncology, driving the development of novel materials and strategies for targeted drug delivery. In this context, receptor-targeted, self-assembling protein nanoparticles represent a versatile platform for selective therapeutic delivery. Exploiting CXCR4 overexpression in a broad range of tumors, the T22 targeting system has shown that multi-domain recombinant protein nanoparticles can selectively accumulate in tumors and elicit potent antitumoral and antimetastatic activity. This approach has generated targeted protein-only nanotoxins and nanoconjugates, achieving receptor-dependent cytotoxicity and therapeutic efficacy *in vivo*.

To extend targeting beyond tumor cells, the platform has been repurposed to address the stromal compartment of the tumor microenvironment (TME), which plays a critical role in tumor progression and therapy resistance. A novel multi-domain protein platform has been developed to target PDGFR-β, a hallmark receptor of cancer associated fibroblasts (CAFs), using its natural human ligand PDGF-D for the first time as a modular targeting domain within a multi-domain recombinant protein system.

The resulting PDGF-D-empowered proteins can be efficiently produced in microbial cell factories, spontaneously self-assemble into functional oligomeric nanoparticles, and exhibit receptor-mediated internalization in PDGFR-β^+ stromal fibroblasts both in vitro and in vivo. While reporter GFP incorporation allows imaging of tumor accumulation in vivo, its replacement with an engineered microbial toxin confers the protein (PDGFD-NT-H6) a potent and selective cytotoxicity toward PDGFR-β^+ cells, resulting in significant tumor growth reduction in murine models. These findings validate the PDGFD-PDGFR-β interaction as a highly selective gateway for the delivery of therapeutic proteins into the TME.

Looking forward, multi-domain recombinant protein nanoparticles offer a modular and highly adaptable platform for precision nanomedicine. Their ability to incorporate diverse functional elements enables the design of multifunctional therapeutic constructs with synergistic effects. By targeting previously unexplored cellular components, this platform opens new opportunities for combinatorial therapies, controlled modulation of the TME, and applications beyond oncology in other disease contexts where selective targeting is critical. As this modular protein concept continues to evolve, it provides a versatile tool for the development of next-generation therapeutics.



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The Raman fingerprint of Salivary Extracellular Vesicles for the differential diagnosis of movement disorders: the MINERVA project

Wednesday, 14th January - 16:20: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 292

Alice Gualerzi [1], ***Luana Forleo*** [1], ***Silvia Picciolini*** [1], ***Valentina Mangolini*** [1], ***Francesca Lea Saibene*** [1], ***Anna Salvatore*** [1], ***Martina Turinelli*** [1], ***Virginia Ambrogi*** [2], ***Alessio Faralli*** [2], ***Elisabetta Farina*** [1], ***Anna Castagna*** [1], ***Gemma Lombardi*** [3], ***Francesca Cecchi*** [4], ***Pietro Arcuri*** [1], ***Marzia Bedoni*** [1]

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Early diagnosis of neurodegenerative diseases is a crucial step in the treatment and care of patients as it allows to tailor prompt personalized therapeutic strategies that can significantly impact on disease progression and on the quality of life of patients and their caregivers. Currently, the importance of biologically based classification of Parkinson's disease and other movement disorders has been clearly recognized, still there is a lack of reliable measurable biomarkers.

The ongoing MINERVA project proposes a method based on the application of Raman spectroscopy to the analysis of saliva-derived Extracellular Vesicles (EVs) on a broad spectrum of neurodegenerative diseases including Parkinson's disease (PD), atypical parkinsonisms (APs), and Alzheimer's disease.

One of the specific aims of the MINERVA project is the validation of a biophotonic-based method for the differential diagnosis of neurodegenerative motor disorders.

To achieve this goal, people with PD and APs were recruited at Fondazione Don Carlo Gnocchi Onlus following the MDS criteria and saliva was collected (Figure1). EVs were isolated from concentrated saliva by size exclusion chromatography and ultracentrifugation. Size, concentration, and protein markers detection (Alix, Flot-1, CD9) assessed the repeatability of the isolation procedure and the homogeneity of the obtained EV population. The Raman analysis was performed on air-dried EVs, casted on calcium fluoride substrates following a previously optimized protocol.

The preliminary results of the MINERVA project demonstrate the ability of Raman spectroscopy to highlight biochemical differences in the protein and lipid content of salivary EVs from PD and APs. Specifically, the Amide I region accounted for major differences, in line with expected variations in the EV-associated protein cargo. The statistical analysis suggested that the differences in the spectral signature of EVs do not correlate with gender and age of the recruited subjects, but allow the discrimination of different movement disorders and correlate with the clinical assessment of the recruited patients.

Once confirmed on the complete MINERVA cohort of more than 240 subjects, the results of the project will represent a turning point in the differential diagnosis of neurodegenerative diseases with significant impact on the personalization of patients' treatment.

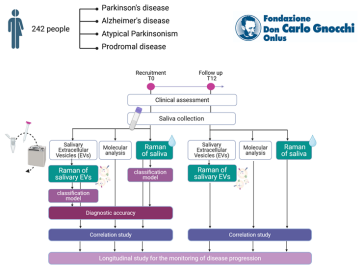

Figure 1. Schematic representation of the study design of the prospective observational clinical trial MINERVA (NCT06869135). Image created in https://BioRender.com

Figure1 minerva project.png

Harnessing Tumor-Derived Extracellular Vesicles to Improve Cancer Cell Identification and Profiling

Wednesday, 14th January - 16:36: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 258

Marta Sevieri [1], ***Ilaria Tagliolini*** [2], ***Beatrice Bignami*** [2], ***Valeria Giacobbo*** [3], ***Francesca Gorgoglione*** [2], ***Arianna Bonizzi*** [2], ***Marta Truffi*** [4], ***Serena Mazzucchelli*** [1], ***Fabio Corsi*** [5]

1. *Department of Biomedical and Clinical Sciences, Università degli studi di Milano, Milan, Italy,* ***2.*** *Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy,* ***3.*** *University of Milan,* ***4.*** *IRCCS Istituti Clinici Scientifici Salvatore Maugeri, Pavia, Italy,* ***5.*** *Breast Unit, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy*

Introduction: Fluorescence-guided surgery (FGS) improves tumor visualization and surgical precision, but a universal cancer-targeting probe is still lacking. A key research goal is to develop biocompatible systems capable of selectively delivering fluorescent dyes like indocyanine green (ICG) to tumor sites. Among emerging strategies, extracellular vesicles (EVs) have gained attention due to their natural role in intercellular communication and their ability to transport bioactive molecules. Their biocompatibility and tumor-targeting potential make them promising candidates for delivering imaging agents during FGS. EVs derived from tumor cells or patient plasma have shown selective affinity for cancer tissues, supporting their use as tumor-tracking vehicles.
Methods: To investigate this potential, we utilized Triple Negative Breast Cancer Patient-Derived Organoids (PDOs) from the B. Boerci oncologic biobank (ICS, Maugeri, Pavia). PDOs were generated by enzymatic and mechanical dissociation of breast cancer tissue samples, and characterized by flow cytometry, immunohistochemistry, confocal microscopy and transmission electron microscopy (TEM) to assess their morphology and histological profiles. EVs were produced by culturing PDOs in Clinostatic incubator for 15 days to stimulate vesicle release (Figure 1). EVs were then isolated using fast protein liquid chromatography with size exclusion (FPLC-SEC). Tumor-derived EVs (T-EVs) were characterized using TEM, nanoparticle tracking analysis (NTA), dynamic light scattering (DLS), and dot blotting to confirm the presence of EV-specific markers.
Results and discussion: The protocol yielded highly pure EVs at a concentration of approximately 3·1010EVs/mL, with a size distribution between 50–150 nm, consistent with known tumor-derived EV profiles. TEM confirmed vesicular morphology, and dot blot validated marker expression such as CD63. ICG was successfully loaded into T-EVs via a 12-hour incubation and ultracentrifugation, producing T-EVs-ICG suitable for imaging. Future studies will assess their tumor-targeting capabilities through binding assays in 2D and 3D cell models, followed by in vivo evaluation of specificity and biodistribution.

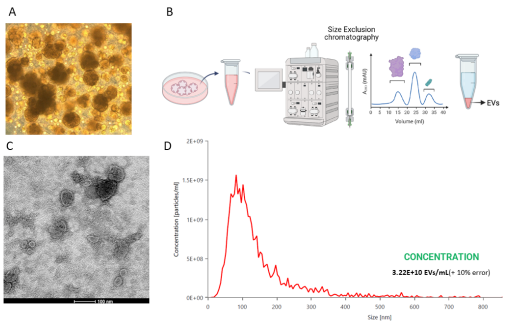

Fig. 1 Isolation of EVs from BC PDO A) BC PDO at day 60; B) Protocol for isolation of EVs from PDO conditioned medium; C) TEM analysis images of EVs extracted from PDOs; D) NTA analysis

Figure1 sevieri.png

Designing biodegradable polymer coatings to modulate DNA origami stability and cellular uptake

Wednesday, 14th January - 16:52: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 252

Santiago Sarasa San José [1], ***Alejandro Postigo*** [1], ***Marina Ripalda*** [1], ***Marcos Sánchez Barat*** [2], ***Laura Ordovás*** [3], ***Jesús del Barrio*** [1], ***Silvia Hernández-Ainsa*** [1]

1. *Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, Zaragoza 50009, Spain,* ***2.*** *Instituto de Investigación Sanitaria de Aragón (IISA), Spain,* ***3.*** *Instituto de Investigación en Ingeniería de Aragón (I3A), Spain*

DNA origami nanostructures have emerged as promising nanocarriers for therapeutic delivery owing to their programmable architecture, biocompatibility, and ability to precisely control cargo loading and release. However, their practical application is challenged by susceptibility to early nuclease degradation and limited cellular internalization.[1]

In this study, we investigated a series of biodegradable and cationic polymers as protective coatings for DNA origami nanostructures (DONs) to enhance their stability and cellular internalization. The polymer series comprised synthetic poly(β-amino ester)s (PBAEs) with systematically varied hydrophobicity, designed to balance colloidal stability, cytocompatibility, and uptake efficiency.

Effective polymer coating on DNA origami was characterized using gel electrophoresis, dynamic light scattering, and transmission electron microscopy. Increasing polymer hydrophobicity led to a transition from individual to aggregated DONs. Enzymatic degradation assays with DNase I demonstrated enhanced protection conferred by more hydrophobic PBAEs. Polymer hydrophobicity also modulated cellular uptake of coated DONs in HEK293 cells, as well as cell viability.

Together, these findings reveal how polymer hydrophobicity critically influences the structural and biological behavior of DNA origami carriers. This work provides design principles for optimizing polymer–DON systems, contributing to the rational engineering of stable, biocompatible, and effective DNA-based nanocarriers for non-viral gene delivery.

The authors would like to acknowledge the funding received, which is associated with the following projects: PRE2021-098521 and PID2020-113003GB-I00 funded by MICIU/AEI/10.13039/501100011033; PID2023-147656OB-I00 funded by MICIU/AEI/10.13039/501100011033 and by ERDF, UE; E47_23R and CNS2022-135887 funded by MCIN/AEI/10.13039/501100011033 and by NextGenerationEU.

[1] Y. Wang, *et al.*, Chemically modified DNA nanostructures for drug delivery, *The Innovation*, Volume 3, Issue 2, 2022, 100217, ISSN 2666-6758

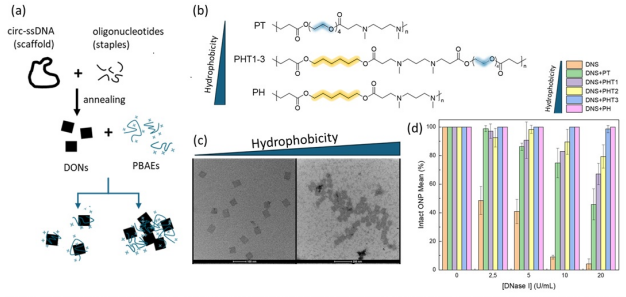

Figure 1. *(a)* Schematic representation of DNA origami nanoparticle formation; *(b)* chemical structures of the PBAE family with varying hydrophobicity used for coating the DNA origami; *(c)* TEM images illustrating the effect of hydrophobicity on polyplex aggregation, as further evaluated through DNase I digestion assays and cellular studies; (d) Stability profile of bare DNA origami and DNA–PBAE hybrids upon exposure to increasing concentrations of DNase I.

Abstract image.jpg

Site-Directed Conjugated Multivalent Protein Nanoparticles for Targeted Drug Delivery into Cancer Stem Cells.

Wednesday, 14th January - 17:08: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 51

Ariana Rueda [1], Annabel Garcia [1], Julian Ignacio Mendoza [1], Lourdes Ailen Arena [1], Ramon Eritja [2], Anna Aviño [2], Carme Fabrega [2], Ramon Mangues [1], Esther Vazquez [3], Antonio Villaverde [3], Isolda Casanova [1], Ugutz Unzueta [1]

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Precision targeting remains a hot topic in cancer nanomedicine, which aims to mitigate the adverse effects caused by the off-target accumulation of cytotoxic drugs in conventional chemotherapies. Although antibody-drug-conjugates (ADCs) are currently the clinical gold standard for targeted drug delivery, their therapeutic performance is still limited by suboptimal biodistribution and off-target drug accumulation [1]. As a promising alternative, we have developed a non-antibody protein-based nanocarrier that self-assembles into stable, biocompatible oligomeric nanoparticles via divalent cation-assisted interactions [2]. This platform integrates a tumor-homing ligand and a histidine-rich architectonic tag into a single polypeptide, yielding nanoscale viral-mimetic particles that avoid renal clearance and exhibit multivalent presentation of the targeting moiety, which supports receptor super-selectivity.

Following this strategy, we constructed a CXCR4-targeted nanocarrier (T22-GFP-H6) displaying multiple copies of the CXCR4-binding peptide T22 [3]. This is highly relevant, as CXCR4 is a chemokine receptor overexpressed in cancer stem cells across more than 20 solid and hematological malignancies [4]. Upon intravenous administration, T22-GFP-H6 nanoparticles achieved exceptional tumor accumulation, with over 85% of the detected signal localized within CXCR4+ tumor [5,6]. Thus, first-generation nanoconjugates, created through covalent binding of different antineoplastic agents (FdU, AraC, MMAE), effectively eliminated CXCR4+ cancer cells in vivo without systemic toxicity [7-9]. However, these nanoconjugates, synthesized via non-specific lysine-amine coupling, showed substantial heterogeneity in drug loading and limited batch-to-batch reproducibility.

To overcome these limitations, we have further engineered a new-generation of nanoconjugates with precise control over the drug-to-nanoparticle ratio (DNR) and exact payload location using site-directed conjugation methodologies [10]. This refined architecture has allowed us to identify the most appropriate drug positioning within the nanocarrier to improve receptor affinity, tumor-selective biodistribution and overall therapeutic performance. Additionally, a humanized version of the nanocarrier was designed to reduce immunogenicity and enhance translational potential [11].

Altogether, the combination of divalent cation-guided multivalent nanoparticle assembly and precision site-specific conjugation strategies enables the production of highly selective, potent, and regulatory-compliant nanomedicines. Thus, this targeted drug delivery system represents a robust platform for the development of advanced precision therapeutics targeting cancer stem cells.

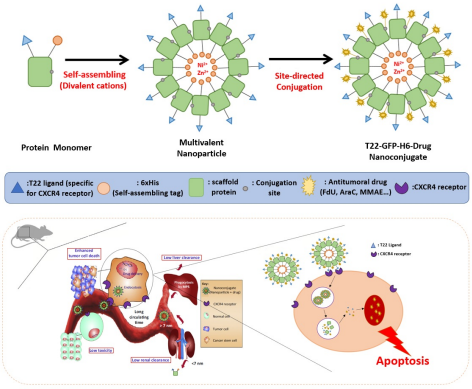

Figure.jpg

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Towards home-based diagnosis: a non-invasive 3-sensor platform for monitoring kidney disease in sweat

Wednesday, 14th January - 17:24: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 223

Giulia Matteoli [1], ***Elena De Gregorio*** [2], ***Lorena Tedeschi*** [1], ***Nicola Calisi*** [3], ***Matteo Mannini*** [4], ***Claudio Evangelisti*** [5], ***Sofia Zanotti*** [1], ***Silvia Ghimenti*** [2], ***Denise Biagini*** [2], ***Tommaso Lomonaco*** [2], ***Claudia Torino*** [1], ***Pietro Salvo*** [1]

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Chronic Kidney Disease (CKD) is a progressive and multifactorial disorder with an increasing global incidence and is currently considered as a major cause of mortality worldwide. In clinical practice, the estimation of glomerular filtration rate (GFR) depends on several biomarkers such as creatinine, which is the gold standard, cystatin C and urea. Cystatin C greatly improves the accuracy of GFR estimation when used with creatinine whereas elevated urea levels may indicate impaired renal clearance. To establish a sensing platform for remote monitoring of patients during daily activities, we developed three sensors for simultaneous detection of creatinine, cystatin C, and urea in human sweat that provide a non-invasive alternative to blood-based testing. Sweat-based monitoring allows for a non-invasive approach for high frequency health monitoring that can support clinicians to assess and manage patients' therapy, thus reducing the number of hospitalizations.

This work presents three electrochemical sensors for the quantification of cystatin C, creatinine, and urea in human sweat. For cystatin C, we developed an aptasensor on a titanium carbide (Ti_3C_2) MXene-based substrate. This aptasensor combines the high specificity of the aptamer with the excellent electrical conductivity of MXenes. The creatinine sensor exploits the electro-oxidation of the copper–creatinine complex by using titanium carbide–copper quantum dots (Ti_3C_2-Cu QDs). The urea sensor is a composite of metal hydroxide nanoparticles engineered to interact specifically with urea. The response of the three sensors was measured by electrochemical impedance spectroscopy (EIS).

The cystatin-C aptasensor had a limit of detection (LOD) of 3.1 ng/mL with an RMSE of 8% in the range of interest 2 – 18.5 ng/mL. The creatinine biosensor worked in the range 10–100 µM, with a LOD of 1 µM and an RMSE of 10%. In the range 50–200 mM, the urea sensor had a LOD of 36 mM and an RMSE of 15%. These results are consistent with literature and meet the clinical specifications for assessing pathological renal conditions.

This work was supported by The European Union through the Horizon Europe EIC programme (Grant Agreement project 101115504).

Rethinking Scientific Instruments: Riding the AI4Science Wave

Wednesday, 14th January - 17:40: Diagnostics and Devices (Room 1) - Invited Speaker - Abstract ID: 325

Xiaobao Cao [1]

1. *Guangzhou Laboratory*

The ongoing technological revolution, centered on artificial intelligence (AI), is profoundly reshaping the landscape of life science. As a pivotal force driving future industrial transformation, bio-manufacturing relies heavily on the intelligence and automation level of its equipment, which directly determines the core competitiveness of the bio-economy. This report aims to explore the new paradigms, opportunities, and challenges emerging in the development of bio-manufacturing equipment under the impetus of the AI wave. It will first explain the inevitable trend of deep integration between AI technology and bio-manufacturing equipment, with a focus on how AI empowers key processes such as high-throughput screening and bioprocess optimization, thereby enabling the transition of equipment from “automation” to “intelligence.” Through specific case studies, the report will showcase cutting-edge advancements in AI-driven antibody development and digital life research. Additionally, it will address critical issues in building an “AI + Bio-manufacturing” research and development system, including challenges such as data silos. Embracing the AI wave and accelerating the intelligent upgrading of bio-manufacturing equipment are essential engines for seizing the strategic high ground in global bio-manufacturing and cultivating new quality productive forces.

TFAMoplex: A modular protein based nanoparticulate system for gene delivery

Thursday, 15th January - 09:00: Plenary Session 1 (Auditorium) - Plenary Speaker - Abstract ID: 310

Jean-Christophe Leroux [1]

1. *ETH Zurich*

Gene therapy holds significant potential for the treatment of a wide range of diseases and is already being applied in several genetic disorders. However, key challenges remain—particularly the safe and efficient delivery of nucleic acids to target cells. Large genetic cargos often suffer from poor cytoplasmic and nuclear access, even after reaching the target tissue. To overcome these barriers, nucleic acids are typically delivered using viral vectors or synthetic nanocarriers, the latter often exhibiting lower transfection efficiencies compared to viral systems. In this presentation, we introduce *TFAMoplex*, a novel protein-based gene delivery platform. It is built upon the mitochondrial transcription factor A (TFAM), which self-assembles into nanoscale particles upon binding to DNA. TFAM can be genetically fused to various functional proteins, such as targeting ligands or endosomolytic enzymes, enabling receptor-mediated uptake and facilitating endosomal escape of the cargo. Under stringent *in vitro* transfection conditions—such as high serum content and brief exposure times—optimized TFAMoplexes achieve transfection efficiencies comparable to those of adeno-associated viral (AAV) vectors. Furthermore, *in vivo* studies demonstrate that TFAMoplexes retain transfection activity following intramuscular injection in mice. However, the observed gene expression was transient under the tested conditions, indicating the need for further optimization of the formulation for sustained effects. This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (grant agreement No 884505).

Roadmap from discovery to early clinical development of mRNA-Lipid Nanoparticles

Thursday, 15th January - 09:40: Plenary Session 1 (Auditorium) - Plenary Speaker - Abstract ID: 279

Marianna Yanez Arteta [1]

1. *Advanced Drug Delivery, Pharmaceutical Sciences, R&D, AstraZeneca, Gothenburg,*

Research on lipid nanoparticles (LNPs) for delivery of mRNA has catapulted in the past years based on their potential to easily adapt to different therapeutic indications. Although there are hundreds of active clinical trials worldwide in this area, the success of many of these trials will depend on ensuring that the discovery efforts can be translated to a product that can be supplied to early clinical studies. LNPs need to be tailored to the specific indication to select the right lipid chemistries and compositions, as well as a suited manufacturing process and control strategy that aligns with the regulatory requirements.

Here, a roadmap towards designing, selecting, and developing an LNP for mRNA therapies will be presented. It will focus on 4 key aspects: Efficacy, Safety, Stability and Manufacturability, and how understanding the fundamental interactions that governs the LNP formation can help us to improve these areas. Building knowledge on structure-activity relationship for mRNA-LNPs supports the foundations to ensure these medicines reach the patients.

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Inorganic nanoparticle-based platforms to tackle cancer

Thursday, 15th January - 10:50: Plenary Session 2 (Auditorium) - Plenary Speaker - Abstract ID: 317

Teresa Pellegrino [1]

1. *Istituto Italiano di Tecnologia (IIT)*

TBA

Multidimensional immunoengineering approaches to enhance cancer immunotherapy

Thursday, 15th January - 11:30: Plenary Session 2 (Auditorium) - Plenary Speaker - Abstract ID: 318

Li Tang [1]

1. *École polytechnique fédérale of Lausanne (EPFL)*

TBA

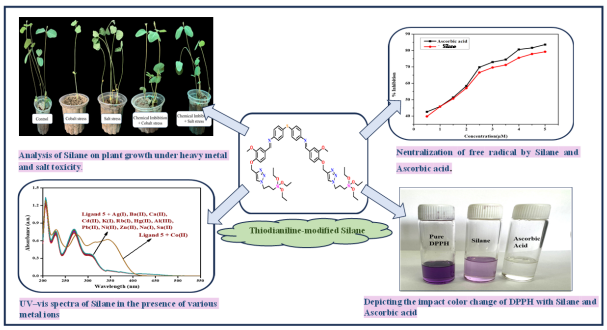
Thiodianiline-modified silane for Co(II) detection and its dual antioxidant and abiotic stress-mitigating potential

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 302

DEVINA SHARMA [1]

1. *a Department of Chemistry & Centre of Advanced Studies, Panjab University, Chandigarh, 160014, India*

Heavy metal contamination is a pressing global concern due to its persistence, bioaccumulation and irreversible toxicity, with Co(II) posing particular environmental and biological hazards even at trace levels. In this study, a 4,4′-thiodianiline-derived triazole-functionalized silane was designed, synthesized and structurally validated using ^{1}H NMR, ^{13}C NMR and mass spectrometry. The synthesized molecular scaffold demonstrated sensitive sensing performance toward Co(II), exhibiting high selectivity with negligible interference from competing metal ions and an impressive limit of detection of 6.5×10^{-8} M. A pronounced downfield shift of the triazole proton from 7.68 to 7.85 ppm in the ^{1}H NMR spectrum confirms robust coordination with Co(II), further supported by DFT calculations. Beyond sensing, the silane displays striking antioxidant activity, evidenced by a visible discoloration in the DPPH assay and a strong IC_{50} value of 1.45 µM. Significantly, biological evaluation under environmentally relevant conditions shows that treated soybean plants maintained superior growth under high salinity and heavy-metal stress, highlighting notable abiotic stress–mitigating potential. Collectively, this multifunctional molecule offers a powerful platform for ultra-sensitive metal ion detection, antioxidant applications and sustainable agricultural resilience.



Conference.png

Antibacterial electrospun wound dressing with flame-made Ag/SiO2 nanoparticles

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 242

Reshma V. Ramachandran [1], ***Jennifer Geara*** [2], ***Maria Samara*** [1], ***Thomas Thersleff*** [2], ***Ning Xu Landén*** [2], ***Georgios A. Sotiriou*** [1]

1. *Stockholm University,* ***2.*** *Karolinska Institutet*

Infections caused by drug-resistant bacteria such as Methicillin-resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa continue to impede effective wound repair [1]. We report an antibiotic-free nanofibrous dressing fabricated by integrating flame-made silver nanoparticles (Ag NPs) into polyvinyl alcohol-chitosan (PVA-CS) electrospun fibers. The Ag NPs (2-10 nm) were generated by flame spray pyrolysis (FSP) [2], an industrially scalable technique enabling tight control over particle composition and size distribution. Embedded within ~200 nm fibers, the nanoparticles are physically immobilized in the polymer matrix, resulting in a stable and continuous release of Ag^+ ions while preventing particle leaching.

Four membrane formulations (PVA:CS = 100:0, 95:5, 90:10, 80:20) were fabricated to study the influence of composition on antibacterial efficacy. The 90:10 and 80:20 membranes achieved >99.9999% bacterial reduction in vitro and up to 99% in an ex vivo human-skin infection model. Both MRSA and P. aeruginosa were effectively inhibited, confirming broad-spectrum antibacterial performance. Cytocompatibility tests demonstrated >90% viability of human keratinocytes and fibroblasts, while histological and immunohistochemical analyses of wounds on excised human skin confirmed preserved tissue integrity and normal healing.

Mechanistic investigations revealed that the combined use of FSP and electrospinning ensures precise nanoparticle size control and uniform dispersion within the fibers, resulting in a stable, sustained Ag^+ release profile from minimal Ag/SiO_2 loading. This design minimizes cytotoxicity and the risk of silver resistance while maintaining potent antibacterial action.

This study introduces a scalable, **safe-by-design nanofiber platform** that integrates industrial nanoparticle synthesis with electrospinning to create antibacterial, biocompatible, and antibiotic-free wound dressings. The approach offers strong translational potential for managing infected wounds and reducing dependence on conventional antibiotics [3].

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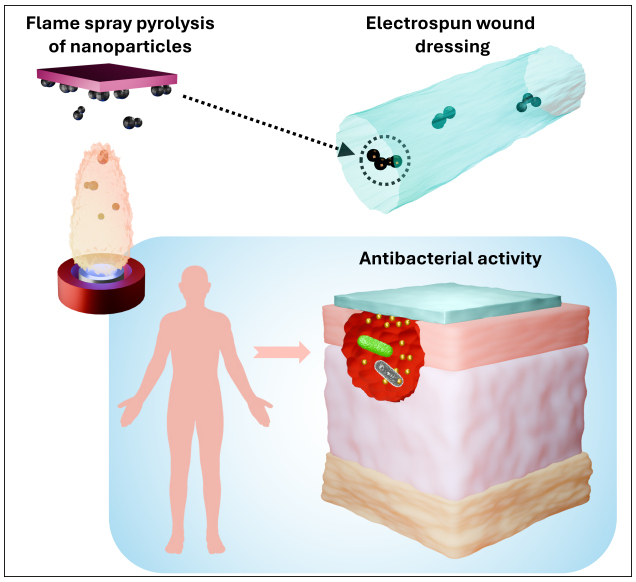

Antibacterial wound dressing.png

Development of Vitamin-E hexosomes as mRNA carriers for CAR-T cell engineering in glioblastoma immunotherapy

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 196

Manuela Zingarelli [1], ***Valerie Sartor*** [2], ***Laure Gibot*** [2], ***Martina Beccalli*** [3], ***Pierangelo Metrangolo*** [3], ***Serena Pellegatta*** [4], ***Barbara Lonetti*** [5], ***Francesca Baldelli Bombelli*** [3]

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Biocompatible Nanoparticles (NPs) have been extensively investigated in the therapeutic field for their potential as drug and gene delivery vectors. In particular, lipid nanoparticles (LNPs) have been used in clinical setting as mRNA-based vaccines and therapeutics. Moreover, LNPs are a promising tool to generate personalized therapies in cancer immunotherapy, such as in the production of CAR-T cells. However, they present some limitations in hard-to-transfect cells such as T cells, as well as in achieving efficient endosomal escape.

The remarkable success of CAR-T cell therapy in treating B cell malignancies has transformed the landscape of cancer immunotherapy. Nonetheless, its effectiveness against solid tumors continues to face significant challenges. Specifically, for glioblastoma (GBM), an untreatable primary brain cancer, phase I clinical studies demonstrated safety, but modest efficacy. Recently, a retroviral-based CAR targeting B7-H3, a membrane protein overexpressed in over 70% of GBM and other cancers, but absent in normal tissues, was developed. B7-H3.CAR-Ts recognize and kill GBM cell lines *in vitro* and increase survival in GBM xenograft models. Despite these encouraging preclinical results, developing engineered CAR-Ts at clinical levels by viral-based gene transfer is costly and logistically challenging as it requires cell factories specifically designed for producing clinical grade viral vectors and transduced CAR Ts.

We propose the use of T cells engineered via non-viral lipid-based mRNA nanocarriers to express a B7-H3.CAR, to demonstrate the efficacy of mRNA-B7-H3.CAR-Ts in a preclinical model of glioblastoma.

Here we show the formulation and characterization of novel NPs based on Vitamin E-derived lipids featuring hexagonal liquid crystalline structure (HEX-NPs), that shall promote fusion with cell membrane and enhance NP intracellular internalization. Nucleic acid (NA) loaded HEX-NPs were decorated with different stabilizers and studied in biological fluids to determine protein corona interactions. These formulations were also tested on different cell lines, including T cells, and showed good viability and different internalization efficiencies depending on the used stabilizer. Overall, these findings establish a promising base for developing the optimal HEX-NP formulation for CAR-Ts engineering by mRNA delivery.

Dynamic Intracellular Trafficking of PAMAM Dendrimers in HEK293 Cells

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 117

Edwind Rojas [1], Diego Cifuentes [1], Carola Díaz [2], Leonardo Guzman [1]

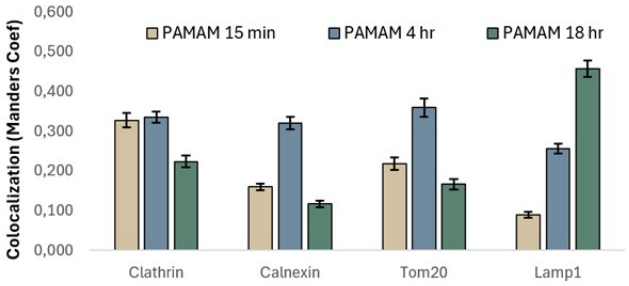
1. *Departamento de Fisiología, Universidad de Concepción,* ***2.*** *Departamento de Ciencias Químicas, Universidad Andrés Bello*

Polyamidoamine (PAMAM) dendrimers are synthetic, tree-structured nanocarriers employed for drug delivery. Their modifiable surface facilitates drug carriage, enhancing therapeutic solubility and efficacy. Moreover, their capacity for cellular internalization enables the intracellular release of their cargo. Consequently, a precise understanding of their intracellular trafficking is essential for guiding their rational design. However, the subcellular distribution of PAMAM dendrimers remains inadequately defined. This study characterizes the localization proximity between internalized PAMAM dendrimers and specific subcellular structures and organelles.

PAMAM dendrimers, covalently modified with fluorescein isothiocyanate (PAMAM-FITC), were used along with one of the following specific antibodies for different cellular elements: Clathrin (endocytic vesicles), Calnexin (endoplasmic reticulum), Tom20 (mitochondria), and Lamp1 (for lysosomes). Both fluorescence signals were registered using confocal microscope. HEK293 cells were incubated with PAMAM-FITC 15 minutes. After washing the cells, fluorescence was monitored after 0 hours, 4 hours, and 18 hours. Manders coefficient was calculated as a measure of colocalization at a resolution of 150 nm. The cellular fluorescence retention associated with PAMAM dendrimer decreased from 20.81 to 17.76 after 4 hours and to 11.54 (RFU) after 18 hours. This reduction may be associated with degradative processes or cellular export.

Regarding the association with Clathrin, colocalization with PAMAM decreased from Manders Coefficient 0.327 ±0.018 at 0 hours to 0.224 ±0.014 after 18 hours. Concerning the association of PAMAM with the endoplasmic reticulum marker Calnexin, it increased from 0.160 ±0.008 to a maximum of 0.320 ±0.0155, to decrease again to 0.117 ±0.007. The relationship with the mitochondrial marker Tom20 also peaked at 0 hour with 0.218 ±0.016, increasing to 0.359 ±0.023 to decreas to 0.167 ±0.013. Finally, the association with the lysosomal marker Lamp1 was particularly interesting, increasing from 0.090 ±0.007 to 0.257 ±0.012 and 0.457 ±0.018 after 4 and 18 hours, respectively.

Thus, we successfully demonstrated that PAMAM associates with different cellular structures in a specific and distinct temporal pattern for each one. It is noteworthy that the association with the endoplasmic reticulum shows a transient peak, whereas PAMAM signal appears to accumulate in lysosomes. These findings could guide the design of such drug delivery systems towards specific subcellular targets.



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Cationic Amphiphilic Hybrid System (CAHS) for siRNA Delivery to Solid Tumors

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 59

Pasquale D'Anna [1], ***Fabiana Quaglia*** [1], ***Claudia Conte*** [1], ***Cameron Alexander*** [2]

1. *University of Naples Federico II, Department of Pharmacy, Naples,* ***2.*** *University of Nottingham*

Nanomedicines and combination therapy are gaining prominence due to their ability to produce synergistic anticancer effects, reduce the toxicity of individual agents, and overcome multidrug resistance (1). Hyaluronic acid (HA) has emerged as a key targeting ligand, enhancing nanoparticle (NP) uptake by CD44-overexpressing cancer cells. This approach can be further advanced by incorporating small interfering RNA (siRNA), offering an innovative tool for cancer therapy (2).

An initial study was conducted to determine the optimal N/P ratio required for effective siRNA adsorption onto the cationic component, represented by the lipid DOTAP. Agarose gel showed complete adsorption at a DOTAP/siRNA weight ratio of 6:1. NPs were prepared using the nanoprecipitation technique. The organic phase (OP) consisted of a water-miscible solvent containing 10 mg of a polymer blend (PLGA and PEG_{2k}-$PLGA_{2k}$) and 1 mg of DOTAP. This OP was added dropwise into water without surfactants, stirred for 30 minutes, followed by solvent removal via rotary evaporation. The final formulation was then functionalized with an outer layer of HA. Hydrodynamic diameter (D_H), polydispersity index (PI), and zeta potential (ζ) of NPs were measured on a Zetasizer Nano ZS (Malvern Instruments), showing a size of 160 nm with a PI of 0.1 (Fig.1A-B), a negative zeta potential (~ 10 mV) (Fig.1B) and a complete adsorption of siRNA. TEM analysis showed a spherical core-shell structure of PEGylated NPs (Fig.1A). Long-term stable NPs were obtained with HPbCD as cryoprotectant (Fig. 1C). RNAse assay showed no siRNA degradation with or without the coating of HA, emphasising the ability of PEG chains to protect siRNA from RNAse degradation (Fig. 1D). Cytotoxicity and cellular uptake were performed in MDA-MB-231 cells overexpressing CD44. NPs exhibit no significant cytotoxicity after 72 h of incubation and at concentrations up to 500 µg/mL (Fig. 1E). Regarding the uptake study, a dose-dependent internalisation was observed (Fig. 1D). Transfection and combination studies based on the co-entrapment of Doxorubicin inside NPs are currently ongoing.

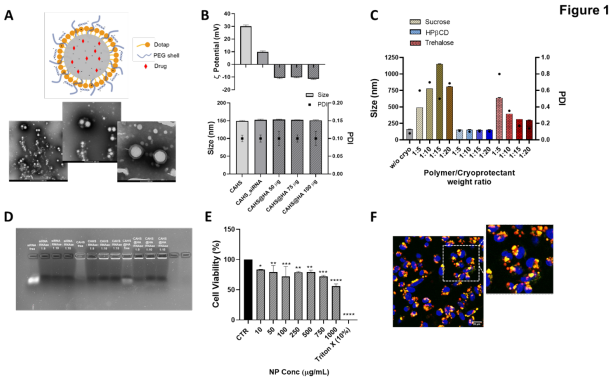

Figure 1. A) Sketch of NPs and TEM images; B) Size and z of the formulations made; C) Freeze-drying studies; D) siRNA adsorption and RNAse assay; E) Cytotoxicity of MDA-MB-231 breast cancer cells after 72h of incubation with NPs; F) Internalisation and endo-lysosomal escape of NPs in MDA-MB-231 breast cancer cells after 48h of incubation (nucleus in blue stained with DAPI; lysosome in green and siRNA in red).

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Biosilica based resolvin D1-nanoformulation in novel therapeutic approaches for unresolved inflammation.

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 311

Alessandra Aloisi [1], ***Matteo Mucci*** [2], ***Riccardo Di Corato*** [1], ***Domenico Mattoscio*** [2], ***Antonio Recchiuti*** [2]

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Inflammation plays a key damaging role on lungs and other organs in cystic fibrosis (CF): it is excessive and never progresses to resolution and tissue repair. In previous work we provided proof of concept that the pro-resolving lipid mediator resolvin (Rv)D1 rectifies intrinsic clinical abnormalities of lung inflammation in CF[1,2]. With the advent of highly effective modulator therapies (HEMT), inflammation resulting directly from lack of CFTR activity is expected becoming less pronounced. However, clinical studies indicate persistent chronic airway infection and inflammation post HEMT treatment and may still cause morbidity.

The ambitious goal of our work is to have engineered a biosilica-based RvD1 formulation that resolves the CF-associated inflammation, which is cornerstone for the therapeutic use of this molecule due to short half-life in vivo.

We manufactured submicron biosilica -hollow nanoporous particles- (SNP), using an optimized sol-gel synthesis in aqueous phase, where spermidine was the amine-bearing molecule able to promote and control silicification, acting both as catalyst and template[3]. RvD1 was loaded in SNP (proved with EIA, HPLC, LC-MS). Dissolution tests demonstrated that RvD1 is constantly (up to 96 h) released from SNP more efficiently in alkaline (intestine-like) than acidic conditions. When SNP-RvD1 (10 ng/mouse) was administered to Cftr KO mice infected with P. aeruginosa significantly reduced weight loss, bacterial titer in lungs, and infiltrated leukocytes and PMN in BAL 24 h post infection compared to SNP (given as a placebo). Remarkably, in side-by-side experiments with wildtype mice, equidose RvD1 (10 ng) did not reduce bacterial load nor leukocytes/PMN numbers in BAL 24 h post infection.

Our work indicates that SNP i) increase RvD1 stability across a wide range of storage temperatures and for long periods; ii) ease RvD1 handling and administration; iii) increase by at least 10x RvD1 efficacy in vivo. Evidence from our studies indicates that RvD1 is a rectifier of CF non-resolving inflammation and that SNP are a suitable formulation to increase RvD1 stability and raising its potency.

[1]E. Isopi et al. Front Immunol. 2020 Apr 28; 11:581

[2]A. Recchiuti et al. Faseb. 2011; 25:544-560

[3]G. Della Rosa et al. Sci Rep. 2020, Dec 3;10(1):21142

Effect of biodegradable nanoparticles on radiosensitization of patient derived cells

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 275

Enza Torino [1], ***Mariarita Menale*** [2], ***Angela Costagliola di Polidoro*** [2]

1. *University of Napoli Federico II,* ***2.*** *University of Naples Federico II*

Biodegradable polymeric nanoparticles to be used as radiosensitizers are obtained through microfluidic nano-precipitation system based on hydrodynamic flow focusing. Synthetic identity and Biological identity are tested GSC1 patient-derived cells and U87. Radiosensitization ability is measured by treating selected cells with nanoparticles followed by ionizing radiation and assessed for clonogenic survival, DNA damage (γ-H2AX foci formation), and reactive oxygen species (ROS) generation. Furthermore, Western blotting analyses are performed to visualize the activation or inhibition of key signalling pathways involved in DNA repair, oxidative stress response, and apoptosis following combined treatment. By combining physicochemical characterization with functional and molecular assays, this approach provides insights into the mechanisms of nanoparticle mediated radiosensitization.

Development and Stability Assessment of 20-Hydroxyecdysone-Encapsulated Ethosomes

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 267

Joanna Czerniel [1], ***Krzysztof Bernady*** [1], ***Dariusz T. Młynarczyk*** [2], ***Ludwika Piwowarczyk*** [3]

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Psoriasis is a chronic inflammatory skin condition that affects approximately 125 million people worldwide. Treatments include topical agents, phototherapy, systemic immune modulators, and biologics, all aimed at relieving symptoms and improving quality of life. However, side effects, treatment resistance, high costs, and individual variability remain challenges. A promising alternative is topical 20-hydroxyecdysone (20HE), a hormone produced by arthropods and also found in plants. Though not hormonally active in humans, 20HE shows anabolic, adaptogenic, hypoglycemic, antioxidant, and organ-protective effects, with emerging anticancer potential. Due to its lipophilic nature, efficient delivery systems are needed. Ethosomes, a type of lipid vesicle with high ethanol content, offer innovative, biocompatible, and biodegradable drug delivery, enabling deep skin penetration. Their composition typically includes phospholipids, ethanol, water, and active substances.
The study aimed to design and develop 20HE-loaded ethosomes. The research focused on selecting the appropriate method for ethosome preparation, optimizing the ingredients, and assessing stability over 28 days.
Materials and methods: Soybean phospholipids of varying degrees of purification, 20HE, water, and ethanol of varying percentages were used to prepare the ethosomes. The reference sample without the active substance was also prepared. The process was carried out using the cold method and the thin-film method.
Results: The cold method proved to be the optimal preparation method. Employing soy lecithin with varying degrees of purification and ethanol with different percentages, ethosomes with an average particle size of 265.4 – 109.0 and 203.0 – 86.7 nm were obtained, characterized by a polydispersity index in the range of 0.393 – 0.088 and 0.316 – 0.085, and a zeta potential in the range of -41.5 to -18.8 and -55.4 to -22.0 mV, respectively, for the reference samples and ethosomes containing 20HE. Stability testing of ethosomed at 4°C showed satisfactory stability for 28 days of storage for formulations composed of highly purified soybean phospholipids.
Conclusions: The developed ethosomes exhibited satisfactory physicochemical properties and stability. These findings support the potential of 20HE-loaded ethosomes, based on highly purified soybean phospholipids, for further research and therapeutic applications.
Funding: This work was funded by grant No. 2024/ABM/03/KPO/KPOD.07.07-IW.07-0043/24-00 from the National Recovery and Resilience Plan, Poland.

Design, synthesis and characterization of AuNPs-based drug delivery systems using natural compounds and biodegradable polymers for cytotoxic and viral applications

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 250

Xavier Siwe Noundou [1]

1. *Department of Pharmaceutical Sciences, School of Pharmacy, Sefako Makgatho Health Sciences University, Pretoria, South Africa*

Cancer remains a major public health problem worldwide in 2025. According to the International Agency for Research on Cancer (IARC), cancer may cause over 11 million deaths worldwide in 2030. Most of cancer's treatments have a low rate of success and have the general disadvantage of unpleasant side effects underscoring needs for novel, cost effective and more efficient cancer treatments as well as their improved delivery strategies. Nanoparticles (NPs) are progressively considered as a potential candidate to carry active principles safely into a targeted site in an organ. In addition, many of the existing anti-cancer drugs are derived from natural products. It is estimated that a large proportion of the global population still depends on traditional, often herbal, medicine for their health needs. Species of Euphorbiaceae family such as *Alchornea cordifolia* have recently been shown to have a number of biological activities including anti-malarial, antibacterial and anticancer. Two natural anticancer compounds named methyl gallate (AC3.1) and stigmasterol (AC2.4) (isolated from *A. cordifolia*) were used as reducing and capping agents in the synthesis of gold NPs (AuNPs). The AuNPs were further encapsulated into two stimuli responsive natural and biodegradable polymers i.e. chitosan and alginate. The natural compounds were characterized using NMR and MS and the synthesized polymeric drug delivery systems (DDS) were characterized using UV-Vis, FT-IR, TEM, SEM, XRD, EDS, DLS and zeta potential.
The obtained metallic NPs showed polymorphic shapes and narrow polydistribution sizes. The mean particle size for AC2.4-AuNPs and AC3.1-AuNPs was 9 ± 2 nm and 13 ± 2 nm, respectively. The polymeric DDS (or nanocarriers) AC3.1@AuNPs-Chitosan, AC2.4@AuNPs-Chitosan, AC3.1@AuNPs-Alginate and AC2.4@AuNPs-Alginate were successfully synthesized and characterized. More interestingly, the structure of the nanocarriers was found to be amorphous, suitable for drug development, and the mean size was established using TEM and DLS and ranged between 52 nm and 164 nm. Also, the size of nanocarriers is suitable for DDS and corroborates with those found in literature for the drug delivery systems. However, the evaluation of the cytotoxicity and viral activity of the nanocarriers needs to be investigated.

Enhanced stability and improved antioxidant potential of lycopene via nanoliposome encapsulation

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 220

Nenad Stojiljkovic [1], ***Sonja Ilic*** [1], ***Natalija Mitic*** [1], ***Nemanja Kitic*** [1], ***Janko Stoiljkovic*** [1]

1. *Department of Physiology, University of Nis, Faculty of Medicine*

Since the lycopene is known to be relatively unstable and its usage is limited due to its hydrophobicity and low availability, its encapsulation in nanoliposomes might significantly increase its application in a range of unique and distinct biological activities. The aim of this study was to evaluate the stability and antioxidant properties of the encapsulated form of lycopene under various experimental conditions.

Phospholipid nanoparticles in the form of nanospheres were dissolved as a 10% solution and encapsulated by lycopene. The encapsulation efficiency, determined spectrophotometrically, was 71.9%. The release kinetics demonstrated a gradual, linear increase during the first 8 hours, with stabilization after 12 hours, when approximately 50% of the total lycopene had been released.

Stability testing in buffer solutions of different pH values (6.4–9.0) showed that lycopene degradation was markedly slower in acidic and neutral media. After 180 minutes of incubation, the residual rate of encapsulated lycopene was 58.2 ± 0.4% at pH 6.4, 53.9 ± 0.0% at pH 7.4, and 20.9 ± 0.18% at pH 9.0, whereas for free lycopene the residual rates were 9.0 ± 0.6%, 4.2 ± 0.3%, and 4.1 ± 0.1%, respectively. These results indicate that nanoliposome encapsulation provides substantial protection against pH-induced degradation. The stability of lycopene in the presence of metal ions (K^+, Ca^{2+}, Mg^{2+}, Al^{3+}, and Cu^{2+}) showed that the residual rates of encapsulated lycopene were 45.3 ± 2.2%, 51.2 ± 2.9%, 38.3 ± 1.7%, 36.2 ± 1.2%, and 48.1 ± 2.1%, respectively, compared to 34.7 ± 1.2%, 38.5 ± 1.6%, 24.2 ± 0.7%, 23.7 ± 0.7%, and 33.3 ± 1.0% for free lycopene. This confirms that encapsulation improves lycopene stability and reduces its interaction with metal ions. Exposure to H_2O_2 revealed that encapsulated lycopene exhibited significantly higher antioxidant capacity compared to free lycopene and empty nanoliposomes, as evidenced by a marked decrease in malondialdehyde (MDA) concentration ($p < 0.01$ and $p < 0.001$, respectively).

Lycopene encapsulation in nanoliposomes provides high incorporation efficiency, sustained and controlled release, provides protection against degradation due to different pH of media and reduces the level of metal chelation, which can potentially allow its wider application.

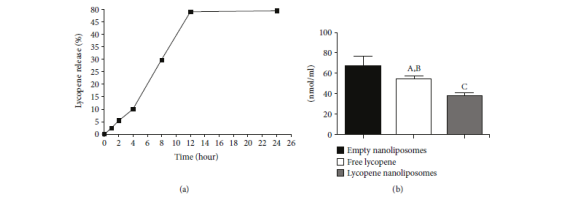


FIGURE 1: Encapsulated lycopene sustained release curve (a) and MDA levels (b) after exposure of free lycopene, empty nanoliposomes, and encapsulated lycopene nanoliposomes to oxidative damage by incubation with H_2O_2. Data are presented as mean value ± SD. $^A p < 0.05$ versus empty nanoliposomes; $^B p < 0.01$ versus lycopene nanoliposomes; $^C p < 0.001$ versus empty nanoliposomes.

Figure 1 stojiljkovic.png

Fullerene - Polyglycerol Amphiphiles: A Novel Approach to SARS-CoV-2 Inhibition

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 88

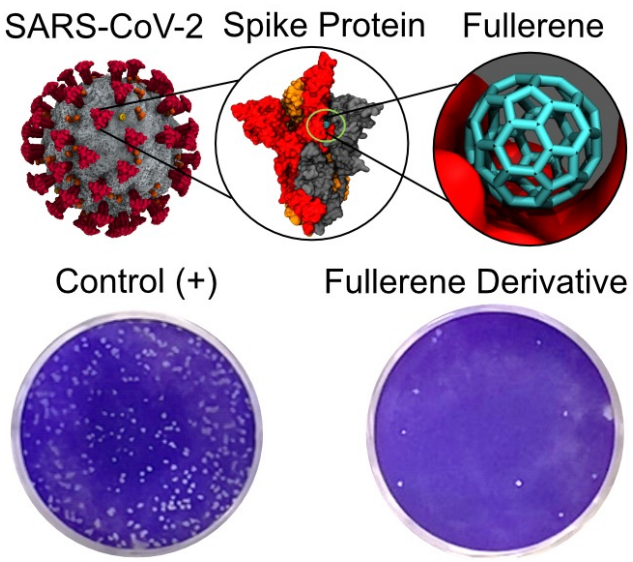
Taylor Matthew Page [1], ***Chuanxiong Nie*** [1], ***Tatyana Povolotsky*** [1], ***Anil Kumar Sahoo*** [1], ***Philip Nickl*** [1], ***Julia Adler*** [1], ***Jörg Radnik*** [2], ***Katharina Achazi*** [1], ***Kai Ludwig*** [1], ***Daniel Lauster*** [1], ***Roland Netz*** [1], ***Jakob Trimpert*** [1], ***Benedikt Kaufer*** [1], ***Rainer Haag*** [1], ***Ievgen Donskyi*** [1]

1. *Freie Universität Berlin,* ***2.*** *Federal Institute for Material Science and Testing - BAM*

Viral infections pose a serious global health challenge, as underscored by the COVID-19 pandemic, which has increased the demand for effective antiviral therapeutics. Nonspecific viral inhibition requires a common mechanism of action or property that can be targeted by synthetic materials.

Here, we present an antiviral amphiphile effective against a broad spectrum of viruses, including multiple strains of SARS-CoV-2, while exhibiting minimal toxicity. Its activity is driven by multivalent electrostatic and hydrophobic interactions. Fullerene-polyglycerol sulfate conjugates demonstrate strong synergistic antiviral effects, combining the high viral affinity of negatively charged heparin analogues with hydrophobic interactions between fullerene moieties and the SARS-CoV-2 S1 protein.

Microscale thermophoresis measurements confirm that linear polyglycerol sulfate binds to the S1 protein, with binding affinity enhanced by fullerene conjugation. All-atom molecular dynamics simulations reveal a hydrophobic pocket on the S1 protein surface that accommodates the fullerene moiety. Additional characterization by atomic force microscopy and cryo-transmission electron microscopy further supports these findings.



Page - antiviral f-lpgs.jpg

Polyglycerol Sulfate Derivatives as Broad-Spectrum Virus Inhibitors

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 142

Taylor Matthew Page [1], ***Chuanxiong Nie*** [1], ***Kai Ludwig*** [1], ***Jakob Trimpert*** [1], ***Katharina Achazi*** [1], ***Klaus Osterrieder*** [1], ***Mohsen Adeli*** [1], ***Rainer Haag*** [1], ***Ievgen Donskyi*** [1]

1. *Freie Universität Berlin*

Multivalency is a key phenomenon in biological systems that enables strong yet reversible interactions through the simultaneous binding of multiple ligands. Nature employs this principle in the glycocalyx, where it facilitates cell-cell recognition and communication. As a feature of cellular surfaces, particularly epithelial cells, the glycocalyx is often exploited by viruses, which use its components such as heparan sulfate (HS) for initial attachment and entry.

When designing broad-spectrum antiviral materials, polyanions such as polyglycerol sulfate (PGS), which mimic HS, emerge as promising candidates due to their minimal toxicity and favorable biocompatibility. The antiviral efficacy of multivalent PGS systems can be further enhanced through conjugation with various motifs, including aliphatic chains, 2D graphene platforms, and fullerene. These amphiphilic components contribute detergent-like interactions with viral envelopes, leading to viral deactivation.

The synergistic activities of electrostatic and hydrophobic forces demonstrate potent antiviral activity, as demonstrated by surface plasmon resonance (SPR) and microscale thermophoresis (MST), alongside plaque reduction, preinfection, and virucidal assays. Effective inhibition has been observed against multiple viruses, including SARS-CoV-2 (wild-type, Beta, Delta, and Omicron variants), feline coronavirus, vesicular stomatitis virus, and respiratory syncytial virus.

Lipid nanoparticle-mediated mRNA delivery to the omentum improves locoregional treatments for peritoneal carcinomatosis

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 103

Ainara Salgado Pascual [1], ***Daniel Moreno-Luqui*** [2], ***Román García*** [2], ***Pedro Berraondo*** [2], ***Fernando Aranda*** [2], ***Sara Zalba*** [1], ***Maria J Garrido*** [1]

1. *University of Navarra,Department of Pharmaceutical Sciences, School of Pharmacy & Nutrition, Pamplona.,* ***2.*** *Cima Universidad de Navarra, Program of Immunology and Immunotherapy, Cancer Center Clínica Universidad de Navarra (CCUN), Pamplona.*

Peritoneal carcinomatosis, characterized by aggressive dissemination of malignant cells within the peritoneal cavity, remains a significant challenge in advanced gastrointestinal and gynecological cancers. Locoregional immunotherapy has emerged as a promising strategy to enhance therapeutic efficacy while minimizing systemic toxicity. In this context, omentum plays a crucial role in orchestrating the antitumor immune response against peritoneal metastases, as it harbors key immune cell populations.

Our previous work demonstrated the potential of mRNA-based therapies to target the omentum and minimize off-target liver effects following locoregional administration. However, this was achieved using TransIT®, a clinically unsuitable transfection tool. Therefore, this studye aims to identify clinically friendly lipid nanoparticle formulation (LNP) for mRNA delivery to the omentum, capable of enhancing the locoregional response observed with TransIT®, and building upon this proof of concept.

A library of 16 LNPs, formulated using the Tamara microfluidic device, was designed, characterized and evaluated for biodistribution against TransIT® in MC38 tumor bearing C57BL/6 mice after a single intraperitoneal administration of 10μg luciferase mRNA. In vivo and ex vivo protein expression was quantified using IVIS imaging system. Finally, flow cytometry was performed to identify the main cell population responsible for the uptake of intraperitoneally administered LNPs in the omentum

The LNPs were successfully prepared and characterized for size, polydispersity index (PDI), surface charge, and encapsulation efficiency (average size 80-150nm, PDI<0.3, ±15mV surface charge, and >80% encapsulation). Luciferase mRNA expression and biodistribution varied among formulations. LNP behavior was highly dependent on composition; for instance, DMG-PEG2K-containing LNPs exhibited greater transfection efficiency than DSPE-PEG2K, while SM102-based LNPs demonstrated higher omentum tropism compared to MC3-based LNPs, which accumulated preferentially in the liver. These findings led to the selection of at least two novel candidates that showed enhanced omentum accumulation and a higher omentum to liver ratio compared to TransIT®. The omentum accumulation was explained by immune cells/LNP interaction, being macrophages the predominant cell population uptaking LNPs.

In conclusion, locoregional LNP delivery demonstrated selective tropism for the omentum, supporting their potential as efficient carriers for intraperitoneal mRNA delivery. Further studies, incorporating therapeutic mRNA, are ongoing to confirm their translational potential.

Design and development of nanomaterials for the intraarticular treatment of osteoarthritis

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 50

Marina Frutos [1], ***Guillermo Landa*** [2], ***Manuel Arruebo*** [2], ***Gracia Mendoza*** [1]

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Osteoarthritis (OA) is a chronic and degenerative joint disease that affects over 250 million people worldwide, with its prevalence rising due to population aging and lifestyle factors. It is characterized by inflammation, cartilage degradation, and pain, which compromise joint structures and significantly reduce quality of life. Current treatments mainly provide symptomatic relief, with limited efficacy and potential adverse effects, underscoring the need for more effective therapeutic strategies.

Resveratrol (RSV), a natural polyphenol found in various plants, has demonstrated relevant anti-inflammatory properties in OA. It partially inhibits the IL-1β-induced NF-κB signaling pathway by reducing the expression of matrix-degrading enzymes such as MMP-3 and MMP-13, and also downregulates pro-inflammatory mediators like TNF-α and iNOS via TLR4-dependent pathways.

To overcome RSV's poor aqueous solubility and limited bioavailability, a nanoparticle (NP)-based drug delivery system was designed. RSV was chemically conjugated to hyaluronic acid (HA), forming amphiphilic HA@RSV conjugates capable of self-assembling into stable NPs. The nanoparticles were characterized morphologically and by size using transmission electron microscopy (TEM). FTIR spectroscopy confirmed the formation of the conjugate, revealing structural differences between HA and HA@RSV, including a more intense peak at 1606 cm^{-1} (due to replacement of HA's carboxyl group by an ester bond), a new peak at 1315 cm^{-1} (indicative of ester linkage), and an increase at 950 cm^{-1} (from additional C–O bonds introduced by RSV).

Anti-inflammatory activity was evaluated in vitro using LPS-stimulated ATDC-5 cells by measuring nitrite production. Working concentrations of RSV and NPs were carefully determined based on prior cytotoxicity assays to ensure cell viability and experimental relevance. Both free RSV and HA@RSV significantly reduced nitrite levels in pre-treatment and post-treatment protocols. Free RSV decreased NO production by 60% (pre) and 50% (post); HA@RSV achieved reductions of 30% and 20%, respectively. Since HA alone showed no significant differences compared to the LPS group, the anti-inflammatory effects observed with HA@RSV can be attributed to the RSV component.

These findings support the potential of the HA@RSV system as a promising strategy for OA treatment, offering sustained anti-inflammatory benefits.

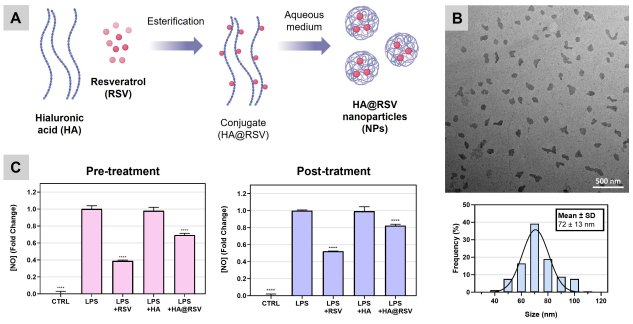


Figure: Design and development of nanomaterials for intra-articular osteoarthritis treatment. (A) Schematic representation of the chemical conjugation involved in the formation of HA@RSV NPs. (B) Image of HA@RSV NPs by TEM and particle size distribution (mean ± SD; n=30). (C) Nitric oxide production by ATDC-5 cells after 4 h pre-treatment or 6 h post-treatment with RSV 1 µg/mL, HA 50 µg/mL, and HA@RSV 50 µg/mL. Data are shown as mean ± SD fold change vs. LPS-treated cells (set to 1); *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001

Marinafrutos figure.jpg

Oxidative stress in liver tissue caused by methotrexate. Effects of encapsulated form of lycopene.

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 221

Sonja Ilic [1], ***Nenad Stojiljkovic*** [1], ***Natalija Mitic*** [1], ***Janko Stoiljkovic*** [1], ***Nemanja Kitic*** [1]

1. *Department of Physiology, University of Nis, Faculty of Medicine*

Methotrexate (MTX) is a chemotherapeutic and immunosuppressive drug known to induce hepatotoxicity primarily through oxidative stress mechanisms. Overproduction of reactive oxygen species (ROS) and depletion of antioxidant defenses lead to lipid peroxidation, protein oxidation, and inflammation, resulting in significant structural and functional liver damage. Lycopene, a natural antioxidant, has been recognized for its strong free radical scavenging properties; however, its limited solubility and instability reduce therapeutic efficacy. Encapsulation of lycopene in nanoliposomes may enhance its bioavailability and protective potential.

The aim of our study was to investigate the effects of encapsulated lycopene on oxidative stress parameters in liver tissue of methotrexate-treated rats. Forty-eight male Wistar rats were divided into eight groups of 6 animals. MTX (20 mg/kg) was administered on the first day. Other experimental groups received MTX combined with empty nanoliposomes (10 ml/kg), lycopene (6 mg/kg), or encapsulated lycopene (6 mg/kg) for 10 days. Corresponding control groups received corn oil, lycopene, empty nanoliposomes, or encapsulated lycopene alone. Biochemical analyses included determination of levels of catalase (CAT), advanced oxidation protein products (AOPP), malondialdehyde (MDA), myeloperoxidase (MPO), and nitric oxide (NO). MTX administration caused a significant decrease in CAT activity (46.6 ± 1.3 IU/mg proteins) and marked elevations in AOPP (29.6 ± 6.1 μmol/mg), MDA (27.5 ± 2.3 nmol/mg), MPO (189 ± 2.3 OD/mg), and NO (65.5 ± 5.8 μmol/L) compared to controls, confirming oxidative stress and inflammation. Co-treatment with lycopene moderately improved these parameters (CAT 60.1 ± 0.1; MDA 17.8 ± 3.1; MPO 159 ± 11.3), whereas encapsulated lycopene restored CAT activity nearly to control levels (75.6 ± 5.9) and significantly reduced AOPP (17.9 ± 1.8), MDA (12.9 ± 0.8), and MPO (141.5 ± 14) values. Encapsulated lycopene also normalized NO levels (41.5 ± 1.3 μmol/L), demonstrating a pronounced antioxidant and anti-inflammatory effect (Figure 1).

The results suggest that encapsulated lycopene effectively ameliorate MTX-induced oxidative damage in liver tissue by enhancing antioxidant capacity and reducing lipid peroxidation. These findings suggest that encapsulation of lycopene in nanoliposomes represents a promising approach to counteract methotrexate-induced hepatotoxicity and may have potential therapeutic applications in clinical practice.

Table 1. Liver tissue oxidative and inflammation related parameters in animals after different experimental treatments

Group/Parameter	CAT (IU/mg proteins)	AOPP (μmol/mg proteins)	MDA (nmol/mg proteins)	MPO (OD/mg proteins)	NO (μmol/L)
Control (corn oil treated)	75.8 ± 6.4	13.5 ± 0.1	9.9 ± 1.0	111 ± 4.6	33.5 ± 4.7
Lycopene	77.5 ± 4.3	13.2 ± 0.5	8.5 ± 2.4	99.5 ± 21.9	43.6 ± 4.5
Empty nanoliposomes	78.7 ± 3.7	13.5 ± 0.4	9.3 ± 2.2	117.5 ± 6.3	27.5 ± 10.0
Lycopene-nanoliposomes	77.3 ± 8.6	12.9 ± 1.6	8.4 ± 1.2	119 ± 1.4	41.6 ± 4.8
Methotrexate	46.6 ± 1.3[a]	29.6 ± 6.1[a]	27.5 ± 2.3[a]	189 ± 2.3[a]	65.5 ± 5.8[a]
Lycopene + Methotrexate	60.1 ± 0.1 [a,b]	21.2 ± 0.4 [a,d]	17.8 ± 3.1 [a,b]	159 ± 11.3 [a,d]	47.8 ± 12.1[b]
Empty nanoliposomes + Methotrexate	30 ± 4.3[a]	28.9 ± 2.6[e]	22.3 ± 4.5[a]	170 ± 13.8[a]	64.2 ± 7.5[a]
Lycopene-nanoliposomes + Methotrexate	75.6 ± 5.9 [b,c]	17.9 ± 1.8[b]	12.9 ± 0.8 [a,b]	141.5 ± 14 [a,b]	41.5 ± 1.3[b]

[a]p<0.001 vs. Control group treated with corn oil; [b]p<0.001 vs. Methotrexate group; [c]p<0.001 vs. Lycopene + Methotrexate group; [d]p<0.01 vs. Methotrexate group.

Figure 1.png

Characterization and Biological Assessment of Lipid Nanoparticles Encapsulating a DNA PPRH Targeting HPV-18 E7 in HeLa Cells

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 288

Roger Fabrega Alsina [1], ***Iria Naveira Souto*** [2], ***Anna Lagunas Targarona*** [3], ***Jessica Malavia*** [4], ***Laia Montell Bonaventura*** [5], ***Carlos J. Ciudad*** [6], ***Elisabet Rosell Vives*** [5]

1. *Pharmaceutical Development, Reig Jofre Laboratories, Barcelona, Spain, Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology, Barcelona, Spain,* ***2.*** *Pharmaceutical Innovation, Reig Jofre Laboratories, Barcelona, Spain; Department of Biochemistry and Physiology, School of Pharmacy and Food Sciences, University of Barcelona, Spain,* ***3.*** *Nanobioengineering Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Barcelona, Spain.,* ***4.*** *Department of Analytical Chemistry, Reig Jofre, Barcelona, Spain,* ***5.*** *Science Department, Reig Jofre Laboratories, Barcelona, Spain,* ***6.*** *Department of Biochemistry and Physiology, School of Pharmacy and Food Sciences, University of Barcelona, Spain*

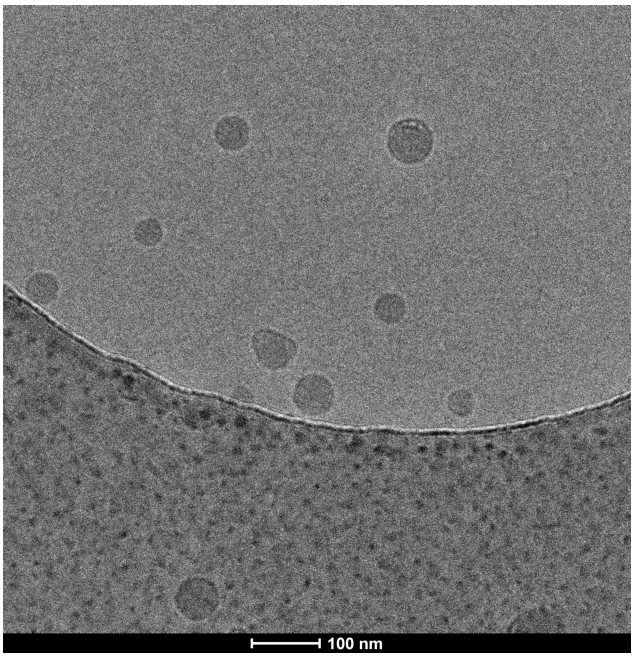
Human papillomavirus type 18 (HPV-18) is one of the most oncogenic high-risk HPV types, associated with cervical cancer development through the expression of viral oncoproteins E6 and E7. In this study, we developed and characterized lipid nanoparticles (LNPs) designed to encapsulate a DNA poly-purine hairpin (PPRH) specifically targeting the E7 gene of HPV-18. The objective was to evaluate their physicochemical properties, encapsulation efficiency, cellular uptake, and biological activity in HeLa cells.

LNPs were prepared using an ionizable lipid-based formulation optimized for DNA encapsulation. Dynamic light scattering (DLS) was employed to determine the hydrodynamic diameter, polydispersity index (PDI), and zeta potential, revealing monodisperse particles with suitable size and surface charge for cellular delivery. Morphological analysis by cryogenic transmission electron microscopy (cryo-TEM) confirmed the presence of spherical, well-defined nanoparticles with a homogeneous size distribution, consistent with DLS data. Encapsulation efficiency (%EE) of the DNA-PPRH was quantified using a Qubit fluorometer, achieving high loading values consistent with efficient nucleic acid complexation.

Cellular uptake was analyzed by flow cytometry after exposure of HeLa cells to fluorescently labeled LNPs, confirming efficient internalization. The biological effect of the PPRH cargo was assessed at the molecular level. Quantitative PCR (qPCR) demonstrated a significant downregulation of E7 mRNA expression.

To evaluate the impact on cell viability, CCK-8 and MTT assays were conducted, showing reduced living cells metabolic activity in treated HeLa cells, consistent with the loss of E7-mediated proliferative signaling.

In summary, our study demonstrates that lipid nanoparticles can efficiently encapsulate and deliver DNA-based PPRHs targeting HPV-18 E7, achieving effective gene knockdown in cervical cancer cells while maintaining suitable morphology, colloidal stability, and biocompatibility. This platform holds promise for the future development of nucleic acid therapeutics against HPV-associated malignancies.



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Development and validation of a gradient HPLC method for the determination of four active pharmaceutical ingredients with antipsoriatic activity properties

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 246

Szymon Tomczak [1], ***Jagoda Szkudlarek*** [1], ***Dariusz T. Młynarczyk*** [2], ***Anna Jelińska*** [1], ***Ludwika Piwowarczyk*** [1]

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Background:
Reliable analytical methods are essential for the characterization and quality control of nanocarrier-based drug delivery systems containing compounds with diverse polarity profiles. This study aimed to develop and validate a gradient high-performance liquid chromatography (HPLC) method for the simultaneous determination of four active pharmaceutical ingredients (APIs), including two hydrophilic (A and B) and two highly lipophilic (C and D) compounds.
Methods:
Chromatographic separation was achieved using a gradient elution system composed of 0.1% (v/v) phosphoric acid in water and acetonitrile as mobile phases. The method employed three different analytical wavelengths in the UV range, selected to match the maximum absorbance of each compound, thereby improving selectivity and sensitivity of detection. The gradient program was optimized to achieve efficient resolution of all analytes within a single analytical run. Validation was carried out according to ICH guidelines for specificity, linearity, precision, accuracy, and robustness. To enable accurate quantification of APIs incorporated in lipid-based nanoformulations such as liposomes and ethosomes, the samples were pretreated to disrupt the lipid matrices prior to analysis.
Results:
The developed HPLC method provided baseline separation of all four APIs with excellent peak symmetry and reproducibility. The use of multiple detection wavelengths ensured selective and accurate quantification of each analyte despite their differing physicochemical properties. Validation results confirmed the reliability of the method across the tested concentration ranges. Application to nanoformulated samples demonstrated the method's suitability for determining encapsulated APIs after appropriate sample preparation.
Conclusions:
The proposed gradient HPLC method, combining optimized chromatographic conditions with multi-wavelength UV detection, offers a selective, robust and versatile analytical approach for the simultaneous determination of hydrophilic and lipophilic APIs not separated so far. Its validated performance and successful application to nanocarrier-based formulations highlight its value for formulation development and routine quality control in advanced drug delivery research.

Funding: *Research aimed at developing a new, innovative pharmaceutical form for the topical treatment of psoriasis vulgaris" is being implemented as part of the National Recovery and Resilience Plan, as part of Investment D3.1.1 Comprehensive development of research in medical sciences and health sciences, reference number: 2024/ABM/03/KPO/KPOD.07.07-IW.07-0043/24-00.*

Pancreatic ductal adenocarcinoma-derived small extracellular vesicles evince different modulation of oxidative responses and the epithelial-mesenchymal transition in hepatic cell models

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 226

Francesco Balestra [1], ***Giorgia Panzetta*** [1], ***Maria De Luca*** [1], ***Federica Rizzi*** [2], ***Roberto Comparelli*** [2], ***Maria Lucia Curri*** [3], ***Gianluigi Giannelli*** [4], ***Nicoletta Depalo*** [2], ***Maria Principia Scavo*** [1]

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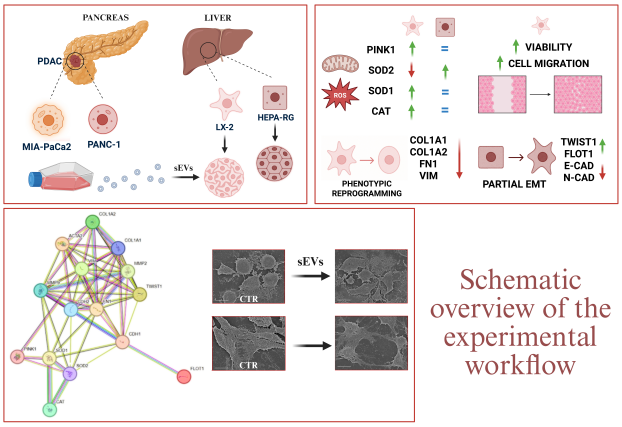
Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive malignancy with early hepatic metastasis and limited treatment options. Small extracellular vesicles (sEVs) released by PDAC cells have emerged as key players in tumor progression, promoting the formation of a pre-metastatic niche. Our study examines how PDAC-derived sEVs regulate oxidative stress, epithelial–mesenchymal transition (EMT), and extracellular matrix (ECM) remodeling in liver cell models: human hepatic stellate cells (LX-2) and human hepatocytes (HEPA-RG). sEVs were isolated from the conditioned media of MIA-PaCa2 and PANC1 pancreatic cancer cell lines and extensively characterized in terms of size distribution, morphology, and the expression of canonical vesicular markers. Their biological impact was then explored through a combination of 2D and 3D functional assays, including cell migration and proliferation tests, comprehensive gene and protein expression analyses supported by bioinformatics tools (STRING), assessment of cellular redox status and mitochondrial performance, and ultrastructural observations by scanning electron microscopy (SEM). Our results reveal that PDAC-sEVs caused significant changes in LX-2 cells, promoting increased viability, migration, expression of oxidative stress enzymes, and ECM-remodeling factors. In contrast, HEPA-RG hepatocytes showed limited migration but exhibited specific redox changes and a “partial” EMT phenotype. Overall, these findings indicate that PDAC-sEVs orchestrate distinct yet complementary responses in different hepatic cell populations: stellate cells undergo oxidative stress adaptation, mitochondrial activation, and matrix-remodeling programs that may facilitate metastatic seeding, while hepatocytes display more restrained but biologically significant redox and transcriptional adjustments. Ongoing research includes extending these observations using sEVs isolated from the sera of PDAC patients to confirm their *in vivo* relevance. Preliminary analyses of patient-derived vesicles have already revealed a molecular signature consistent with tumor origin and aggressiveness. Ongoing experiments aim to validate their functional effects on liver models, thereby bridging the gap between *in vitro* and clinical settings. These translational efforts may ultimately contribute to the identification of novel vesicle-based biomarkers and the development of innovative therapeutic or preventive strategies targeting early metastatic events in pancreatic cancer.



Schematic overview 1 .jpeg

Lithium delivery to tumor cells for neutron capture therapy through targeted carbon nanocarriers

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 185

Esperanza Medina-Gutiérrez [1], ***Rubén García Fontarosa*** [1], ***Marina Llenas Martínez*** [1], ***Valeria Pascali*** [2], ***Alessandro Somenzi*** [2], ***Nicoletta Protti*** [2], ***Gerard Tobias-Rossell*** [1]

1. *Institute of Materials Science of Barcelona (ICMAB-CSIC),* ***2.*** *Università degli Studi di Pavia*

Neutron capture therapy (NCT) is a hadrontherapy modality that relies on isotopes (such as ^{10}B, ^{157}Gd, ^{6}Li), with high neutron-capture cross section, that are able to capture thermal neutrons thus producing highly energetic particles, inducing cell death. It is considered a hybrid, binary cancer therapy, as its therapeutic effect requires the convergence of both the neutron capture agent, and the external neutron beam (*Fig. 1.a*). Nevertheless, selective delivery of current therapeutic agents to cancer cells is still an unmet medical need, and a main challenge for NCT transfer to clinical practice.

Here, we show the therapeutic potential of carbon nanoplatforms for the delivery of ^{6}Li to cancer cells. ^{6}Li is a neutron capture agent that is being explored as an interesting, feasible alternative to currently employed ^{10}B. In this case, active ^{6}Li salts are introduced into previously developed carbon nanohorns (CNHs) functionalized with a targeting agent towards head and neck cancer cells.

Along with neutron autoradiography showing high neutron capture potential of ^{6}Li-loaded CNHs, targeted CNHs were selectively internalized into tumor cells, according to several in vitro techniques, with no associated cytotoxicity (*Fig. 1.b*). Additionally, an increased retention in tumor site in vivo, over other lithium formulations, was revealed by ICP-MS. Regarding their therapeutic potential, ^{6}Li-loaded CNHs and subsequent irradiation with a neutron beam induced a dramatic decrease in clonogenic ability in terms of survival fraction. Consistantly, a preliminary experiment with mice shown decreased tumorogenic ability of cancer cells treated with Li-NCT over non-treated, control cells and neutron-irradiated cells.

While more thorough research must be performed, this novel approach has shown to be a feasible, effective way to deliver ^{6}Li to act as active NCT agents for the delivery of therapeutic doses to cancer cells, having also been protected through a patent (WO2023180615). This will ultimately accelerate the development and implementation of Li-NCT for an improved management of difficult-to-treat tumors through a binary, highly targeted treatment, minimizing damage to healthy tissues.

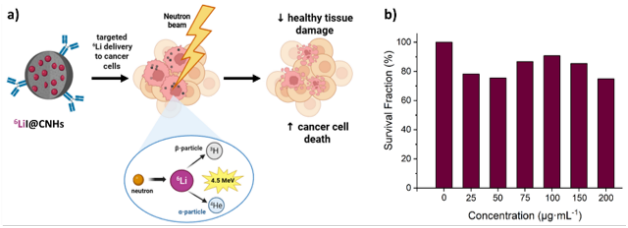


Figure 1. a) Schematic representation *of the antitumor effect upon neutron irradiation of ^{6}Li atoms delivered by NPs inside cancer cells, leading to the formation of nuclear species and, subsequently, specific cell death.* ***b) Clonogenic ability*** *of head and neck cancer cells upon exposure to non-cytotoxic, targeted ^{6}Li@CNHs.*

Figure 1.png

3D-Printed Iron Oxide Nanoparticle Tablets: Hematological, Biochemical, and Immunophenotypic Evaluation in C57BL/6J Mice

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 260

Gabriel Ribeiro Farias [1], ***Heloisa Antoniella Bráz de Mello*** [2], ***Isadora Florêncio de Souza*** [3], ***Mac-Kedson Medeiros Salviano Santos*** [4], ***Idejan Padilha Gross*** [5], ***Marcílio Sergio Soares Da Cunha Filho*** [6], ***Marcelo Henrique Sousa*** [4], ***Sônia Nair Báo*** [1]

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Iron Oxide Nanoparticles (IONPs) are widely applied in biomedical research. A critical factor in IONP clinical applications is the biodistribution profile, biocompatibility, dose administration and the time of retention and clearance by the reticuloendothelial system. This system is composed of the liver, which plays a central role in IONP degradation and iron metabolism regulation, and the spleen, which processes and stores iron, both mediated by macrophages. Structural properties of IONPs, such as core size, surface coatings, and surface charge define the balance between stability and clearance. However, conventional formulations are limited by gastrointestinal adverse effects, which depend on the administered dose. Therefore, precise dose adjustment is often required among patients. In this context, three-dimensional (3D) printing of customized drug delivery systems emerges as a promising strategy, enabling the production of patient-specific doses and release profiles. This study was performed to assess the biodistribution and toxicity of IONP3D in mice. For that, IONPs were synthesized via co-precipitation and coated with citrate, and then extruded into a polymeric matrix made of Polyvinyl Alcohol using hot-melt extrusion and printed as 3D tablets. Then, C57Bl/6J mice were orally administered with 0,026 mg/g and euthanized after 24 h. After that, blood was collected to perform hematological and biochemical analyses, followed by spleen and lymph node excision, to assess the dynamics of macrophage recruitment, by flow cytometry. Hematological parameters showed no significant differences between groups. Similarly, no significant differences were observed in serum AST, ALT, creatinine, or urea levels. Looking at the myeloid-lineage immune cells ($CD11b^+$ single-positive), tissue-resident macrophages ($F4/80^+$ single-positive), and monocyte-derived or activated macrophages ($CD11b^+F4/80^+$ double-positive), the positive control group exhibited a significant increase, which indicates enhanced macrophage recruitment and activation. Treatment with IONP3D resulted in a significant increase only in the frequency of monocyte-derived macrophages. No significant differences were observed in lymph nodes, supporting that this response is spleen-specific, consistent with its role in systemic iron homeostasis. Together these findings suggest good biocompatibility and minimal systemic toxicity. Therefore, we hypothesize a delayed or altered iron metabolic response compared to the positive control, which will be further investigated through functional assays of iron metabolism.

A

Treatment Groups	WBC *(10^3/µL)	Lymph# *(10^3/µL)	Mon# *(10^3/µL)	Gran# *(10^3/µL)	Lymph (%)	Mon (%)	Gran (%)
Control	5,3 ± 1,57	4,6 ± 1,36	0,1 ± 0,06	0,6 ± 0,15	87,6 ± 0,32	1,9 ± 0,20	10,5 ± 0,15
IONP 3d	4,3 ± 1,42	3,6 ± 1,27	0,1 ± 0,00	0,5 ± 0,15	85,0 ± 0,95	2,4 ± 0,49	12,5 ± 0,56
IONP	4,6 ± 1,35	3,9 ± 1,21	0,1 ± 0,00	0,6 ± 0,15	85,5 ± 1,19	2,1 ± 0,40	12,3 ± 1,30
PS	5,8 ± 1,76	4,9 ± 1,73	0,1 ± 0,06	0,7 ± 0,12	84,2 ± 4,65	2,5 ± 1,12	13,3 ± 3,53
P-value	0,6459	0,6756	0,8182	0,3787	0,4301	0,69	0,3863

B

Treatment Groups	RBC *(10^6/µL)	HGB (g/dL)	HCT (%)	MCV (fL)	MCH (pg)	MCHC (g/dL)	RDW (%)
Control	8,9 ± 0,49	13,4 ± 0,72	42,0 ± 2,22	47,4 ± 0,21	15,1 ± 0,06	31,9 ± 0,17	14,1 ± 0,17
IONP 3d	9,4 ± 0,14	14,4 ± 0,46	44,3 ± 0,78	47,4 ± 0,20	15,3 ± 0,42	32,4 ± 0,93	14,2 ± 0,40
IONP	9,3 ± 0,25	14,1 ± 0,31	44,2 ± 0,85	47,4 ± 0,38	15,0 ± 0,12	31,8 ± 0,12	13,3 ± 0,30
PS	9,2 ± 0,24	14,0 ± 0,35	44,0 ± 0,62	48,1 ± 1,21	15,2 ± 0,21	31,8 ± 0,55	14,2 ± 0,78
P-value	0,2436	0,1652	0,1609	0,948	0,4301	0,4415	0,1141

C

Treatment Groups	PLT *(10^3/µL)	MPV (fL)	PDW	PCT (%)
Control	1008 ± 36,5	4,6 ± 0,15	15,6 ± 0,20	0,467 ± 0,009
IONP 3d	984 ± 56,8	4,7 ± 0,12	15,7 ± 0,26	0,458 ± 0,017
IONP	1105 ± 8,1	4,6 ± 0,10	15,6 ± 0,06	0,508 ± 0,014
PS	1039 ± 239,9	4,7 ± 0,06	15,6 ± 0,15	0,490 ± 0,109
P-value	0,671	0,5386	0,7907	0,6912

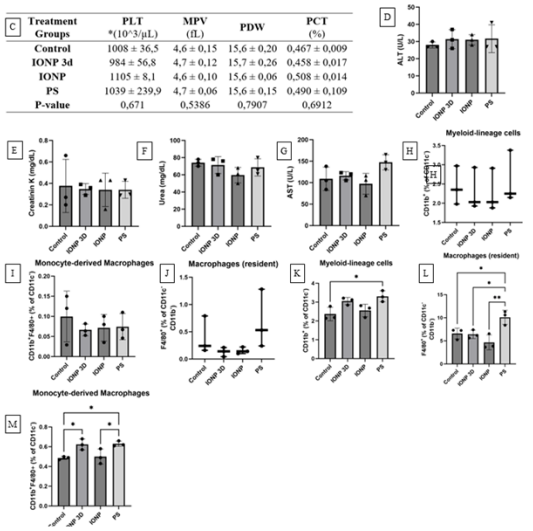


Figura 1 - Hematological, biochemical, and immunophenotypic evaluation of C57BL/6J mice treated with IONP3D. *(A–C) Hematological parameters: (A) total and differential white blood cell counts, (B) red blood cell indices, and (C) platelet parameters. (D–G) Serum biochemical parameters: (D) ALT, (E) creatinine, (F) urea, and (G) AST levels. (H–J) Flow cytometric analysis of macrophage subpopulations in lymph nodes: (H) myeloid-lineage cells (CD11b⁺), (I) monocyte-derived macrophages (CD11b⁺F4/80⁺), and (J) resident macrophages (F4/80⁺). (K–M) Flow cytometric analysis of macrophage subpopulations in spleen: (K) myeloid-lineage cells (CD11b⁺), (L) resident macrophages (F4/80⁺), and (M) monocyte-derived macrophages (CD11b⁺F4/80⁺). Data are presented as mean ± SD. *P|< 0.05; *P < 0.01.*

Hematological biochemical and immunophenotypic evaluation of c57bl6j mice treated with ionp3d..png

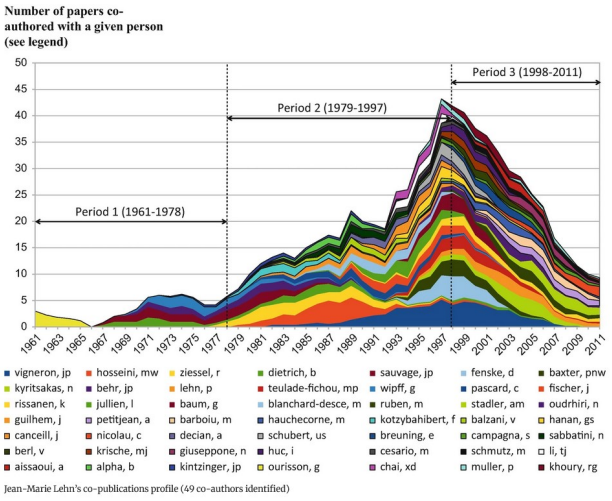
“Not smallness but complexity of biological systems”. The emergence of supramolecular chemistry at the University of Strasbourg (1961-2011).

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 230

Marianne Noel [1]

1. *LISIS*

This communication describes the emergence of a research specialty (supramolecular chemistry or SMC) at the University of Strasbourg over a period of fifty years. The emergence of SMC was orchestrated to a large extent by Nobel laureate Jean-Marie Lehn (1987), but a network of scientists, as well as the University and the Alsace Region, were also key players in this regard. After demonstrating its relevance and formalizing its concept in 1978, Lehn proposed a term to designate a chemistry in which molecules assemble to form supramolecular structures. He argued that self-organisation goes from chemistry to nanotechnology, but from the interface with biology, with the complexity of biological systems, whereas the manufacturing approach defended in nanotechnology is more on the side of physics. Lehn’s approach was to consider that it’s not the smallness that counts, but rather the complexity of the object, and that it is better to build systems that set themselves up. He was also instrumental in the creation of a series of European chemistry journals in the late 1990s, whose genealogy I trace. My purpose is to examine the conditions of the success of a case of European integration that is not a major technological program but simply a “publication infrastructure”. Based on an historical analysis completed with a fieldwork study, I first suggest that beyond the creation of a journal labelled as European, it is the combination of national publication infrastructures, and the processes of articulating and disarticulating them that contributed to the sense of Europeanness that emerged in our fieldwork study. I argue that the circulation and appropriation of numerous concepts, material artifacts and languages of the SMC were central in the development of this European “publication program”, thus laying the foundations for the construction of a European chemical learned society (EuCheMS) created in 2018.



Graphical abstract.jpg

A novel method for rapid, accessible, and cost-effective therapeutic drug monitoring

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 90

Timothy Luxton [1], ***Robert Schnell*** [2], ***Jonathan Sandoe*** [1], ***Lars Jeuken*** [3], ***Christoph Wälti*** [1]

1. *University of Leeds,* ***2.*** *Karolinska Institutet,* ***3.*** *Universiteit Leiden*

Personalising dosing, or therapeutic drug monitoring (TDM), involves measuring drug and adjusting dosing to reach an optimal drug concentration for an individual patient. TDM can be used to reduce side-effects and improve therapy. A challenge for TDM is accessibility of testing. Drug measurement often requires high performance liquid chromatography (HPLC) coupled with mass spectrometry (MS). This limits drug testing to centralised specialist laboratories with the necessary equipment, facilities, and expertise. The need for centralised labs introduces delays to sample-to-result times due to sample transport, high assay cost, and challenges in communicating data. These challenges can limit accessibility and the effectiveness of TDM interventions.

We have developed a new approach for small molecule measurement that enables the sensitive and rapid measurement of small molecules using commonly available lab equipment, with the potential to be further developed to a point-of-care system. We are able to measure our exemplar molecule, meropenem, to therapeutically relevant concentrations in serum and plasma samples using standard laboratory equipment. Our 15-minute wash-step-free test is capable of detecting meropenem in serum and plasma samples using a phone camera, demonstrating the accessibility of the technology and demonstrating the potential for translation to a point-of-care test.

The underpinning technology is generalisable to many small molecule drugs, opening the door to rapid and sensitive TDM at any clinical setting. This provides an opportunity to offer TDM to more patients, especially those who do not have access to state-of-the-art analytical facilities, to reduce toxicities and improve patient care.

Heterogeneity in lipid nanoparticle uptake and transfection and impact of serum content and corona formation on their cell behavior

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 15

Heba Fayyaz [1], ***Anna Salvati*** [1]

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LNPs have emerged as versatile vectors for the delivery of nucleic acid-based drugs. Although they facilitated the introduction of the first RNA therapies to the market, there are still many aspects of the way they interact with cells and deliver their load that remain unclear and/or require further optimization. Here, we used standard 4 component LNPs encapsulating large RNA molecules with a lipid composition similar to Onpattro™, and studied their interaction and biological effects on HeLa cells across a range of concentrations and incubation times. LNPs encapsulating either poly-A or eGFP-mRNA were prepared via microfluidic mixing and included a fluorescently labelled lipid, DiI, to enable quantification of uptake by cells. The LNPs were characterized by dynamic light scattering and zeta potential measurements upon dispersion in water, PBS, and cell culture medium supplemented with serum in order to test their stability in biological conditions. Flow cytometry was utilized to determine their uptake and transfection efficiency in HeLa cells. Moreover, SDS-PAGE was used to compare the composition of the adsorbed corona proteins upon dispersion in serum, as well as how it varied depending on LNP concentration. We found that after a linear increase with LNP concentration, uptake decreases at higher LNP dose . When comparing the amount and identity of the adsorbed corona proteins, we found that different protein amounts were adsorbed at increasing LNP concentration, possibly contributing to the observed lower uptake at higher LNP doses. Additionally in cells with the highest uptake of LNPs, a decrease in cell viability was observed. Finally, we identified a subpopulation of cells which seems more sensitive to the LNPs and compared their uptake and transfection efficiency in respect to the main cell population. Overall, our results showed peculiar trends on the effects of LNP concentration on cellular uptake, transfection efficiency, cell viability as well as protein corona composition. Ongoing studies are aiming at elucidating further the mechanisms behind these observations.

Decoding the pancreatic tumor microenvironment: from matrix stiffness to non-invasive metabolic sensing in 3D in vitro models

Thursday, 15th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 203

Federica Carnevali [1], ***Stefania Forciniti*** [2], ***Anna Chiara Siciliano*** [2], ***Valentina Onesto*** [2], ***Roberta Bove*** [2], ***Helena Iuele*** [2], ***Enza Lonardo*** [3], ***Marcello G. Spampinato*** [4], ***Giuseppe Gigli*** [5], ***Loretta L. Del Mercato*** [2]

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Abstract:

Pancreatic Ductal Adenocarcinoma (PDAC) remains one of the most intractable malignancies, owing to its late diagnosis, extensive stromal remodelling, and resistance to therapy. These challenges arise in part from the complex nano–bio interactions within the tumor microenvironment (TME), where biophysical cues and metabolic gradients converge to drive cancer progression and treatment failure [1-2]. To better recapitulate and interrogate these dynamics, we developed complementary three-dimensional (3D) bioengineered *in vitro* models that integrate ECM-mimetic characteristics and embedded sensing technologies, providing a more physiologically relevant platform for PDAC research.

In the first study, we developed collagen type I-based organotypic scaffolds to investigate how matrix stiffness regulates pancreatic stellate cell (PSC) activation and tumor–stroma communication. Immortalized PSCs, in both monoculture and co-culture with human pancreatic cancer cell lines (AsPC-1 or PANC-1), displayed stiffness-dependent cytoskeletal remodelling, nuclear elongation, and increased α-smooth muscle actin (α-SMA) expression, hallmarks of fibroblast-like activation. Co-cultures further revealed mechano-biochemical feedbacks between stromal and cancer cells, highlighting the role of ECM mechanics in orchestrating PDAC tumorigenesis [3].

A second platform integrates ratiometric optical pH sensors within alginate-based matrices to monitor extracellular acidification dynamics in patient-derived PDAC tumorspheres. This sensing-integrated system enables non-invasive, time-resolved pH mapping at single-cell resolution, capturing distinct metabolic signatures in response to chemotherapeutics including FOLFIRINOX, gemcitabine, and paclitaxel [4]. The resulting metabolic profiles correlated with treatment efficacy, uncovering patient-specific vulnerabilities linked to microenvironmental acidity [5].

Taken together, these studies converge toward deeper understanding of PDAC progression, where microenvironmental stiffness and metabolic reprogramming jointly affect therapeutic response. These platform offers a rapid, scalable tools for personalized drug screening and unveils the role of metabolic heterogeneity and mechanical cues in PDAC chemoresistance.

Foundings: The research leading to these results received partial funding from the ERC under the European Union's Horizon 2020 research and innovation programme (No 759959, ERC-StG "INTERCELLMED", No 101212914, ERC-POC "HySENSE").

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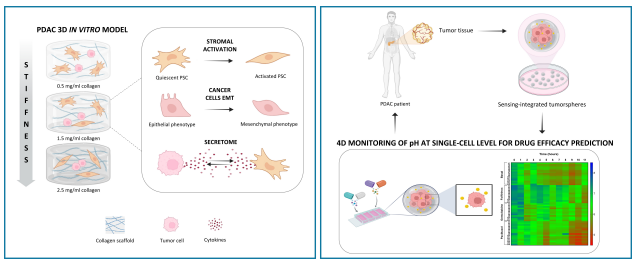
[5] Forciniti S. et al. (under review)



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Injectable Alginate–Hyaluronic Acid Hydrogels Loaded with Light-Activated Nanoparticles for Enhanced Antimicrobial Wound Therapy

Thursday, 15th January - 14:30: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 251

Clara Gamba [1], Virgilio Piccolo [2], Cinzia Reverberi [3], Maria Cristina Ossiprandi [3], Lisa Elviri [4], Claudia Conte [5], Ovidio Catanzano [1]

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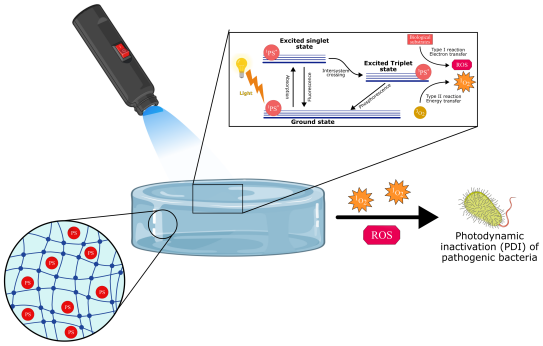
Photodynamic therapy (PDT) has emerged as a promising clinical approach for treating wounds complicated by biofilm-associated infections, where pathogens display increased resistance to conventional antibiotics. When combined with nanotechnology-based strategies, PDT offers enhanced antimicrobial efficacy and wound-healing potential. In this study, we present the development of an innovative light-activated hydrogel wound dressing designed to delivery photosensitizer-loaded nanoparticles (PDT-NPs), enabling controlled modulation of inflammation and broad-spectrum antibacterial activity (Figure 1).

PDT-NPs loaded with the hydrophobic photosensitizer Methyl Pyropheophorbide-a (MPPa), a chlorophyll-a derivative, were fabricated using the emulsion/solvent diffusion technique. Poly(ε-caprolactone) (PCL) and PCL–poly(ethylene glycol) (PCL-PEG) were employed in different ratios to improve nanoparticle stability and biocompatibility. The resulting PDT-NPs exhibited an average hydrodynamic diameter of ~100 nm, low polydispersity, and a negative zeta potential (~−30 mV), independent of PEG content. The production yield reached nearly 100%, indicating the absence of precipitation or aggregation during formulation. MPPa was efficiently encapsulated within the nanoparticles, achieving an entrapment efficiency above 80%. UV–Vis and fluorescence analyses showed that PDT-NPs retained the characteristic optical features of free MPPa in organic solvent, confirming successful encapsulation and effective singlet oxygen generation from the NPs.

PDT-NPs were incorporated into alginate/hyaluronic acid (HA) injectable hydrogels prepared via in situ gelation using glucono-δ-lactone and nanostructured $CaCO_3$, ensuring uniform structure and rapid gel formation. A systematic optimization identified suitable parameters for hydrogel preparation through simultaneous extrusion using a mixing nozzle, yielding transparent, mechanically stable gels forming in less than one minute. HA content influenced both gelation time and crosslinking density. The hydrogels were thoroughly characterized, confirming uniform PDT-NP distribution and effective singlet oxygen generation in simulated wound fluid.

The alginate/HA injectable hydrogels loaded with PDT-NPs exhibited high transparency and uniform nanoparticle dispersion, making them suitable for targeted photosensitizer delivery and in situ activation at the wound site. Ongoing studies are evaluating their in vitro antimicrobial efficacy and biocompatibility.

We acknowledge financial support from the National Recovery and Resilience Plan (NRRP), Mission 4, Component 2, Investment 1.1, under the PRIN 2022 PNRR project “ALADDIN – Advanced Light ActivateD nanoparticle-based wound DressINgs.”



Injectable alginate hyaluronic acid hydrogels loaded with light-activated nanoparticles for enhanced antimicrobial wound therapy.png

PASylated ferritin nanotracers for enhanced tumor imaging and in vivo stability

Thursday, 15th January - 14:46: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 245

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Ferritin nanocages (HFn) offer a promising platform for targeted drug delivery and tumor detection due to their unique architecture and natural tumor-homing ability. In this study, we investigated the potential of an indocyanine green-loaded (ICG) HFn nanoformulation as a tumor-specific nanotracer for fluorescence-guided surgery (FGS). To enhance the stability and circulation time of the nanotracer, HFn was genetically modified by inserting proline, alanine, and serine (PAS)-rich sequences at the N-terminus of each subunit, along with a tumor metalloproteinase-cleavable linker, generating HFn-PAS. Characterization by Transmission Electron Microscopy (TEM), Dynamic Light Scattering (DLS), and Circular Dichroism (CD) confirmed the successful assembly of HFn-PAS nanocages with uniform morphology and size. Encapsulation of ICG within the nanocages produced the HFn-PAS-ICG complex, which exhibited enhanced loading efficiency compared to wild-type HFn. The *in vitro* performance of HFn-PAS-ICG was evaluated in 2D cell cultures using 4T1-Luc murine breast cancer cells and in 3D patient-derived organoids (PDOs). PASylation was found to temporarily inhibit TfR1-mediated interactions with cancer cells, which were restored upon PAS removal. *In vivo*, the biodistribution and imaging performance of HFn-PAS-ICG were assessed in murine models of breast and colorectal cancer. Notably, HFn-PAS-ICG demonstrated significantly higher fluorescence accumulation at tumor sites, with approximately a threefold increase in signal intensity compared to controls in the breast cancer model. Comparable enhancement was observed in the colorectal cancer model.

Overall, HFn-PAS-ICG shows strong potential as a tumor-targeted nanotracer for FGS, combining improved stability, enhanced payload capacity and superior imaging performance. These findings highlight PASylation as an effective strategy to optimize the *in vivo* circulation and efficacy of ferritin-based nanotracers, broadening their applicability in cancer diagnostics and image-guided therapy.

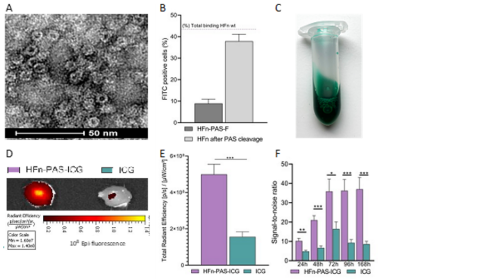

Figure 2 *In vitro characterization and in vivo evaluation of HFn-PAS-ICG. A) TEM analysis of HFn-PAS; B) Binding at 4 °C with 4T1 cells with HFn-PAS and HFn after PAS cleavage (100µg/mL); C) Batch of HFn-PAS-ICG; D) Accumulation at the tumor mass after 1 week; E) Quantification of the accumulation at the tumor mass **p<0,0003; F) Signal-to-noise ratio at 24,48,72,96 and 168h *p=0,01; **0,001<p<0,007; ***0,0005<p<0,0001. The bars are the mean value ± standard deviation (SD), n = 6.*

Hfnpas40 characterization iconan 2026.png

Smart dendritic silica nanostructures for targeted 5-fluorouracil delivery in colorectal cancer

Thursday, 15th January - 15:02: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 224

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This study reports the design, synthesis, and evaluation of dendritic core-shell mesoporous silica nanostructures (SiO_2MSN) designed as a targeted drug delivery system for colorectal cancer (CRC) therapy. The nanoparticles (NPs) feature a non-porous silica core embedding luminescent carbon dots[1] for *in vitro* optical tracking, surrounded by a dendritic mesoporous silica shell with radial, enlarged pores enhancing 5-Fluorouracil (5FU) loading and controlled release. Surface functionalization with polyacrylic acid (PAA), a pH-sensitive polymer, allowed minimal drug release under acidic gastric conditions and triggered release at the near-neutral pH of the colon, ensuring site-specific delivery. Conjugation with an antibody against the Frizzled 10, highly expressed in CRC cells but absent in healthy tissues conferred selective CRC targeting[2]. Physicochemical characterization confirmed nanostructure morphology, pore architecture, and surface modification. *In vitro* experiments with normal (HCEC-1CT) and cancerous (CaCo-2) cell lines demonstrated enhanced uptake of antibody-functionalized NPs in CRC cells, leading to increased cytotoxicity and apoptosis at reduced 5FU concentrations while sparing normal cells. Proliferation marker (Ki-67) and cytoskeletal protein (Vimentin) analyses indicated effective antiproliferative effects and architecture disruption in cancer cells. Cell cycle studies revealed G2/M phase arrest after treatment with targeted NPs. *In vivo* evaluation using the azoxymethane-dextran sulfate sodium (AOM-DSS) mouse model showed that targeted 5FU-loaded NPs at tenfold lower doses than standard chemotherapy substantially reduced tumor burden, notably large polyps, and preserved colon tissue integrity. Immunohistochemical analyses revealed decreased Ki-67, increased apoptosis, and elevated CD68-positive macrophage infiltration, indicating strong antitumor activity and microenvironment modulation. This multifunctional nanostructure innovatively combines structural design, smart polymer gating, and molecular targeting to enhance chemotherapy efficacy and safety. It represents a promising oral therapeutic strategy for CRC, supporting further preclinical and clinical development.

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2. M.P. Scavo et al., *Pharmaceutics* 12 (2020)

Acknowledgements: This work was financially supported by TITAN, Project ID: PONARS01_00906|(PVO-704), Bilateral Project CNR-RFBR Russia Joint research project (2021-2024), NHYLODEA (PRIN 2022 PNRR, code P2022RLFZB CUP H53D23007980001)

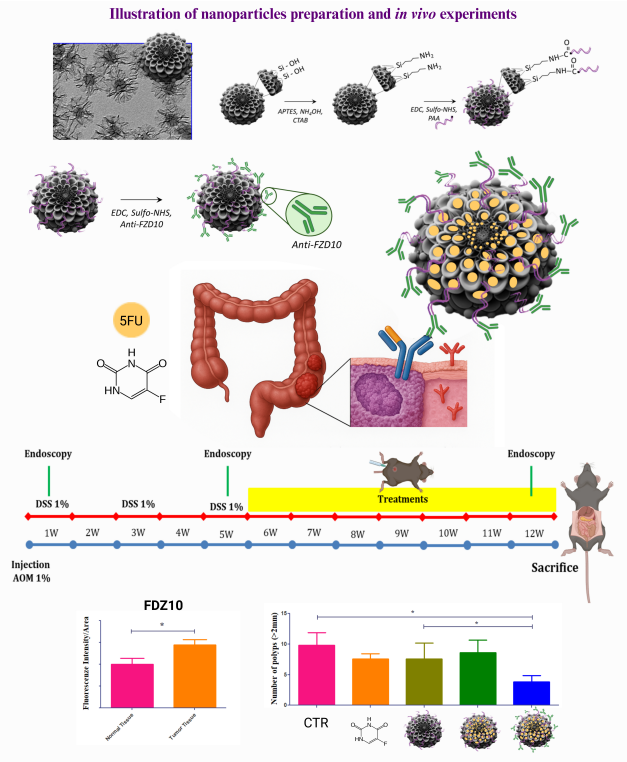

Illustration of nanoparticles preparation and in vivo experiments scavo 1 1 .jpeg

Engineered sonodynamic therapy for CTCL: A tuneable, nanoparticle-enhanced alternative to Extracorporeal Photopheresis

Thursday, 15th January - 15:18: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 210

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Patients with cutaneous T cell lymphoma (CTCL) have been routinely treated since the 1980s using Extracorporeal Photopheresis (ECP). This established procedure involves collecting the buffy coat, adding a phototoxic drug, and applying UV light before reinfusion. A primary limitation of ECP is the lack of treatment personalization: clinical efficacy is only qualitatively assessed by a physician, and the monthly treatment is not quantitatively adjusted based on specific cellular analysis.

Our goal is to develop a customizable therapeutic alternative by substituting UV light with a tuneable low-intensity sonodynamic treatment (SDT). This enables therapy personalization based on patient samples. This SDT tunability is crucial for clinical efficacy, as CTCL is characterized by a high load of circulating malignant T cells. Since the percentage of cancerous T cells is highly variable among patient samples, our adjustable system is engineered to meet the unique, patient-specific requirements for effective tumor cell elimination (Fig1).

Buffy coats from CTCL patients are treated with varying ultrasound intensities and durations. Efficacy is quantified via flow cytometry, monitoring T and B cell markers and tumor cell apoptosis. We establish optimal SDT parameters by comparing cell killing effects against ECP-treated samples over 96 hours. Furthermore, we introduce nanoparticles (NPs) as sonosensitizers, safe alone but triggered by ultrasound to enhance tumor cell killing.

The literature reports that clinical efficacy of reinfused ECP-treated cells stems from induced immunogenicity. Similarly, SDT is able to achieve Immunogenic Cell Death (ICD) by promoting Damage-Associated Molecular Patterns (DAMPs) production, which ensures a strong, active anti-tumor immune response upon reinfusion. Therefore, our alternative and customizable treatment is strongly based on this crucial immunological concept. Results show that increasing power densities of the SDT treatment induce a selective killing of T cells, achieving an apoptotic level of the remaining cells which is comparable and even higher than the ECP standard-of-care. The combination of SDT and NPs further enhances the tumor killing effect, ensuring a high production of DAMPs able to trigger ICD once reinfused.

These findings demonstrate an engineered and customizable alternative to ECP, paving the way for personalized SDT to treat CTCL.

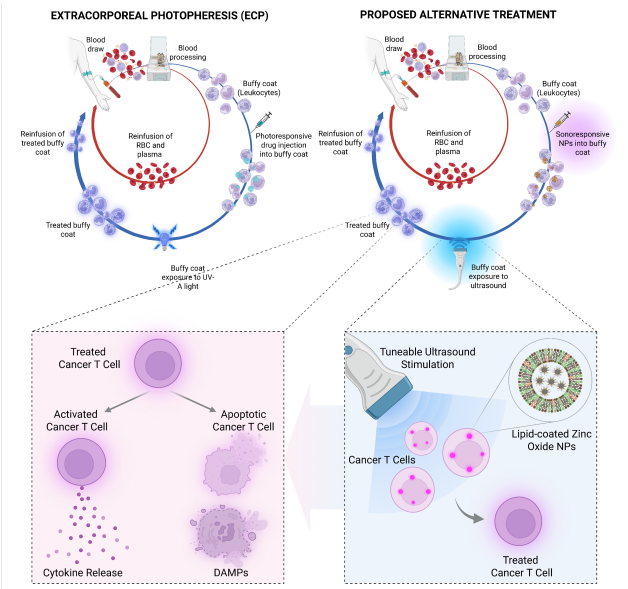

Figure 1. Schematic comparison of the conventional Extracorporeal Photopheresis (ECP) protocol and the proposed Sonodynamic Therapy (SDT) alternative for CTCL. Insets detail the tuneable ultrasound enhanced by nanoparticles (NPs) sensitization and the resulting Immunogenic Cell Death (ICD) of malignant T cells.

Figure1.png

Protein oxidation versus protection: Evaluating the competing duality of metallic nanozymes

Thursday, 15th January - 15:34: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 208

Saad Megahed [1]***, Luca Boselli*** [1]***, Pier Paolo Pompa*** [1]

1. *Istituto Italiano di Tecnologia (IIT)*

Nanozymes are nanomaterials that mimic the catalytic activity of enzymes, with potential applications in various areas of research, spanning from materials science to biological and environmental applications, thanks to their size tunability, facile synthesis, wide operational range, and versatile catalytic activity. Metallic nanozymes NZs, in particular, exhibit multifunctional activities, exerting the activity of both antioxidant (i.e., Catalase-CAT) and pro-oxidant (i.e., Oxidase-OX, Peroxidase-POD) enzymes. The potential application of metallic NZs as therapeutics is attracting increasing interest mainly in virtue of their antioxidant behavior (ROS scavenging), showing protective functionality against oxidative stress in several biological models, both *in vitro* and *in vivo*. Nevertheless, similar NZs have also been reported to perform anti-tumor effects through pro-oxidative action. This functional duality necessitates a thorough investigation to clarify potential collateral reactions, particularly when NZs are deployed as protective agents. In this work, we assessed the potential impact of multifunctional metallic NZs (namely, Au, Pt, and Pd NZs) against proteins using different analytical techniques, including spectroscopic, electrophoretic, and chemical assays. At physiologically relevant H_2O_2 concentrations, none of the NZs induced significant protein oxidative damage. However, at elevated H_2O_2 levels, a material-dependent effect was observed; Pt and Pd NZs predominantly exhibited antioxidant CAT-like behavior, protecting proteins from damage. In contrast, Au NZs led to substantial protein oxidative damage via POD-like activity. These findings underscore the critical importance of material selection and reaction/environmental context in determining the therapeutic efficacy and safety profile of nanozymes.

Ligand Effects of Atomically Precise Au25 Nanoclusters in the Application of Photothermal therapy

Thursday, 15th January - 14:30: Emerging Concepts and Technologies (Room 1) - Oral - Abstract ID: 281

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1. *Marie Skłodowska-Curie Postdoctoral Research Fellow at iLM, CNRS*

Non-invasive photothermal therapy (PTT) has emerged as a promising therapeutic method for the treatment of cancer, where real-time temperature monitoring is critical for clinical efficacy.[1] This promotes the design and development of photothermal agents with accurate temperature control and excellent photothermal conversion. Here, we investigate how the efficiency of light-to-heat conversion can be modulated by changing the surface ligands of thiolated gold nanoclusters (Au NCs; $Au_{25}(SR)_{18}$). Furthermore, the developed nanoheaters show excellent temperature sensing based on fluorescence lifetime. Atomically precise $Au_{25}(SR)_{18}$ NCs (SR = 4-mercapto benzoic acid (pMBA), glutathione (SG), N-acetyl-cysteine (AcCys), captopril (Capt)) were synthesized and fully characterized by high resolution mass spectrometry as well as fluorescence and absorption spectroscopy. The photothermal effect of the NCs was evaluated using a thermal infrared imager (FLIR) to record the temperature change of the aqueous solution of NCs at different concentrations under 808 nm laser irradiation (2 W cm^{-2}, 15 min). The value of photothermal conversion efficiency (η) was calculated using Roper model.[3] $Au_{25}(SR)_{18}$ NCs showed quite pronounced characteristic absorption peaks at 450 and 670 nm, and of particular interest is the remarkable absorption in the 800-900 nm range, which makes them suitable for near-infrared excitation in PTT. The temperature of the $Au_{25}(Capt)_{18}$ solution with a concentration of 0.11 mM rapidly increased to 50 °C within 15 minutes during irradiation with 808 nm continuous laser, and the photothermal conversion efficiency (η) was calculated to be 41.13 %. To show the effect of ligands on photothermal efficiency, the temperature changes under the same conditions were compared, and it was found that the light-to-heat conversion efficiency was in the order Capt> AcCys> SG> pMBA (Fig. 1A). Furthermore, the $Au_{25}(SR)_{18}$ NCs were applied in the study of photothermal therapy using Hela cells and they exhibited excellent photothermal activities in achieving cell death at a power of 9 W/cm^2 using an 808 nm laser source, indicating great potential of $Au_{25}(SR)_{18}$ nanoclusters for cancer phototherapy.

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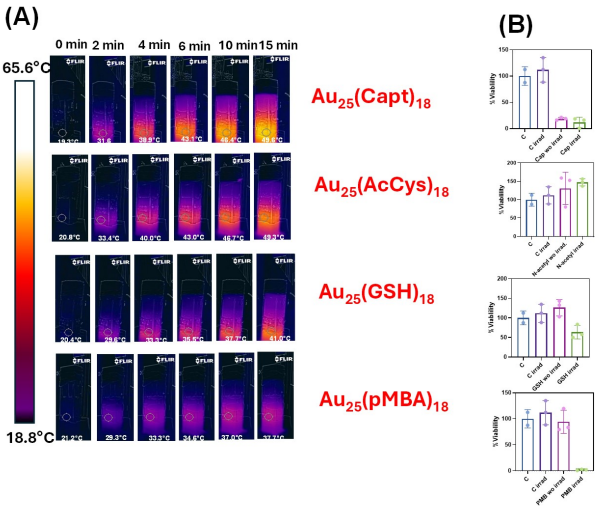


Figure 1. Photothermal effect in (A) solution and (B) Hela cells in $Au_{25}(Capt)_{18}$, $Au_{25}(AcCys)_{18}$, $Au_{25}(SG)_{18}$ and $Au_{25}(pMBA)_{18}$ NCs.

Presentation1 iconan.jpg

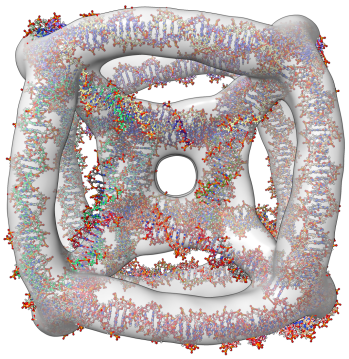
Acoustic Assembly of DNA Wires with an Ultrastable DNA Tesseract

Thursday, 15th January - 14:46: Emerging Concepts and Technologies (Room 1) - Oral - Abstract ID: 276

Julian Tanner [1]

1. *The University of Hong Kong*

Biologically responsive conductive circuitry would lead to a plethora of diagnostic and therapeutic modalities. Nucleic acids have potential for such responsive wiring and circuitry, yet strategies are needed for robust long-range conductivity and wire formation. Acoustically controlled DNA nanostructure assembly is one supramolecular approach yet needs stronger nanostructure building units to withstand acoustic forces during wire formation. Here, we have designed, characterised and assembled a new underlying DNA nanostructure formed from 16 short oligonucleotides into a nested cube we term a DNA tesseract. We solve the DNA tesseract structure by cryoEM, and show that the tesseract structure has thermal and mechanical stability exceeding other DNA nanostructures. These properties allow for fine shaping by surface acoustic waves into a new class of sub-millimetre length DNA wire. The DNA wire shows high conductivity and robustness, opening up significant possibilities for bioelectronics. The DNA tesseract structure has further potential for a wide range of applications in drug delivery, cryoEM structural determination, and ultrasensitive diagnostic electrochemical response.



Tesseractmolecular.png

Design and validation of few shot learning for the prediction of novel synthesized ionizable lipids

Thursday, 15th January - 15:02: Emerging Concepts and Technologies (Room 1) - Oral - Abstract ID: 190

Lasse Hagedorn [1]***, Felix Sieber-Schäfer*** [2]***, Leon Reger*** [2]***, Olivia M. Merkel*** [2]

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Introduction:
Lipid nanoparticles (LNPs) are powerful carriers for nucleic acid delivery, yet their efficiency remains limited by poor endosomal escape, with less than 2% of RNA reaching the cytosol[1]. Since ionizable lipids largely govern this process, their optimization is crucial[2, 3]. To accelerate ionizable lipid design, we developed and validated a meta-learning (ML) model capable of predicting novel lipid structures. Unlike conventional high-throughput screening (HTS) or literature-based ML approaches, our strategy efficiently explores new chemical spaces while maintaining data consistency and biological relevance.
Results:
In this study, we screened a set of 15 LNPs with different synthesized ionizable lipids for their ability to deliver siRNA and mRNA into various cell lines. Different acrylates were obtained by esterification of the respective alcohols with acryloyl chloride. Acrylates were then used to synthesize different ionizable lipids via a solvent-free aza-michael reaction with polyamine head groups. The crude ionizable lipids were dissolved in ethanol with cholesterol, 1,2-Distearoyl-sn-glycero-3-phosphocholine and DMG-PEG2000 and mixed with siRNA or mRNA using a high-throughput microfluidic device. Particles were dialyzed overnight against PBS and characterized for size and PDI.
To compare transfection efficiency across different cellular environments, Firefly luciferase knockdown was quantified in reporter cell lines (H1299, MDA231) (Figure 1a), while mRNA-mediated luciferase expression was analyzed in epithelial (H1299, A549, MDA231) and dendritic (DC2.4) cells (Figure 1b), representing both barrier and immune-relevant models. This allowed us to create a small dataset of high- and low-performing performing LNPs with labeled data for different cargos to train our model.
The pretrained meta-model was subsequently fine-tuned using a support set of nine lipids. The fine-tuned model was then employed to predict lipid performance across all cargo types and cell lines using a five-fold cross-validation approach (Figure 1c) .
Discussion:

Our few-shot learning approach reliably predicted new data across multiple tasks using minimal input, reducing both literature-based noise and avoiding the need for high-throughput screening. This enables more efficient formulation development by minimizing costly prescreening, such as in vivo experiments, and is especially useful in low-data molecule discovery when only a few data points are available.

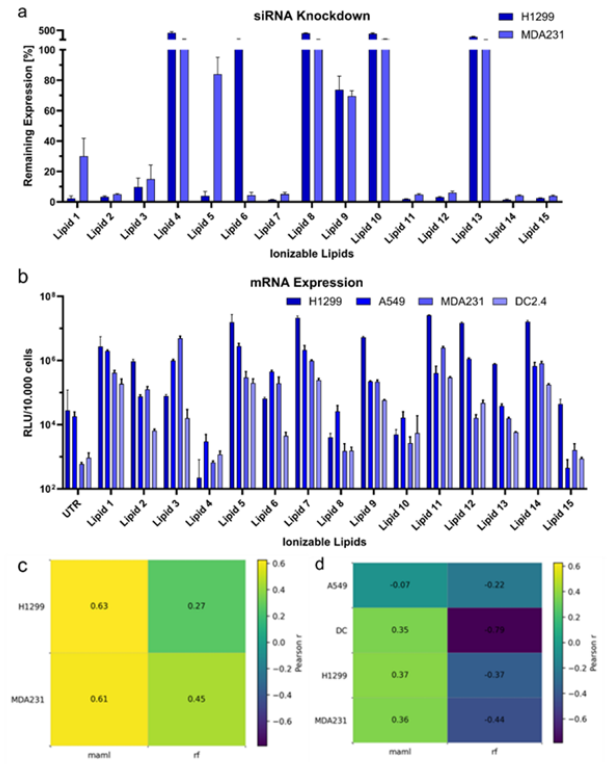

Figure 1. a) Remaining luciferase expression in reporter H1299 and MDA231 cells after treatment with the LNP formulated with the synthesized ionizable lipids. Cells were treated with LNPs for 48 h with 50 pmol of firefly luciferase siRNA and knockdown was normalized to untreated cells. b) Luciferase expression in H1299, A549, MDA231 and DC2.4 cells after treatment with the LNP formulated with the synthesized ionizable lipids. Cells were treated with LNPs for 48 h with 150 ng of firefly luciferase mRNA and expression was log normalized. Results of the few shot model (maml) vs a RandomForrest Baseline (rf) for siRNA (c) and mRNA (d) data.

Lipids screening and ml results final.png

From Copolymer Topology to Thiol-Based Biofunctionalization: Advancing Targeted Nanomedicines

Thursday, 15th January - 15:18: Emerging Concepts and Technologies (Room 1) - Oral - Abstract ID: 110

Francesco Cellesi [1]

1. *Politecnico di Milano*

The rational design of polymer architectures and their chemoselective functionalization represent powerful tools to advance next-generation nanotherapeutics[1-2]. In this work, we present a synergistic approach that combines design-by-architecture strategies with click-enabled postpolymerization modification to tailor the physicochemical and biological performance of polymeric nanocarriers. Using linear and brush block copolymers incorporating poly(ε-caprolactone) and hydrophilic methacrylate derivatives, we demonstrate how architectural variations dictate nanoparticle self-assembly, size, and drug loading efficiency[3]. Brush block copolymers, in particular, enable the formation of smaller, more stable nanoparticles with superior drug encapsulation, while thiol-mediated disulfide crosslinks further enhance structural robustness and enable mucoadhesive interactions via selective binding to mucins.

Complementing this architectural control, we introduce a versatile thiol–epoxy click chemistry platform for postpolymerization modification of glycidyl-bearing polymers[4]. Utilizing TCEP as a disulfide-reducing agent, we achieve highly chemoselective conjugation of biorelevant sulfhydryl molecules, including amino acids and peptides, under mild conditions. This methodology affords multifunctional nanocarriers with tunable hydrophilicity and bioactivity, exemplified by sequential modification with thioglycerol and peptides. The resulting nanoparticles exhibit controlled sizes and targeted biointeractions, expanding the design space for precision nanomedicine.

Together, these studies underscore the potential of integrating macromolecular design with chemoselective functionalization to deliver tailored, stable, and bioactive polymeric nanoparticles (Figure 1). Such strategies hold promises for enabling the next wave of nanotherapeutics, from vaccines to oncology, by bridging rational polymer chemistry with biologically relevant functionality.

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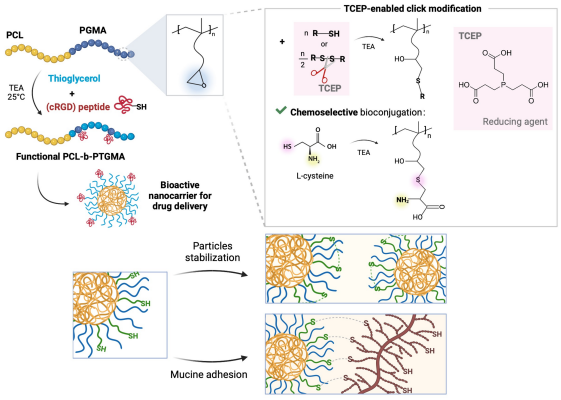

Figure 1. Rational design of polymer architectures with subsequent chemoselective functionalization. Adapted from refs. [3] and [4].

Figure 1 caption.jpg

Synthesis and bioanalytical application of chiral gold nanoparticles in pELISA

Thursday, 15th January - 15:34: Emerging Concepts and Technologies (Room 1) - Oral - Abstract ID: 76

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ELISA (Enzyme-Linked Immunosorbent Assay), a commonly used laboratory test, relies on the antibody–antigen interaction for qualitative and quantitative detection of proteins.
TNFα (tumor necrosis factor alpha) was selected as a model analyte due to its low concentration in biological fluids and well-established analytical protocols, and it is also one of the key biomarkers commonly investigated in the presence of inflammatory conditions.
To overcome the limit of detection (LoD) limitations of standard ELISA, anisotropic, morphologically chiral gold nanoparticles were employed in a plasmonic ELISA (pELISA). The shift of the plasmon band, resulting from etching (oxidation) of gold atoms on the nanoparticle surface, was correlated with the TNFα concentration in the sample. Changes in the amplitude of the CD signal were recorded using a CD spectrophotometer. Morphological changes of the nanoparticles before and after etching were visualized using SEM and TEM microscopy.
A clear correlation between the amplitude of the CD signal and the TNFα concentration was observed. Changes in nanoparticle morphology after etching were confirmed by SEM imaging.
The study demonstrates that morphologically chiral gold nanoparticles can lower the LoD of ELISA-type assays. Such nanoparticles offer potential as a tool for detecting low concentrations of biomolecules, with TNFα serving here as a model analyte.

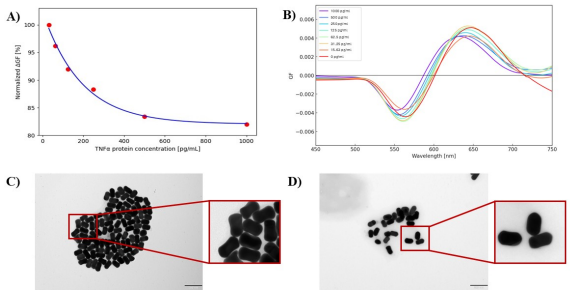

Fig. A) Graph of the relationship between TNF-α concentration and normalized ΔGF (mean of three experimental runs). Red dots represent the averaged data points; the blue line shows the single-exponential fit (ΔGF = a · e^{b · [TNF-α]} + c). **B)** GF spectra at different TNFα concentrations (0–1000 pg/ml). TEM images of the chiral gold nanorods **C)** before and **D)** after the etching process.

Mh fig.jpg

Metabolically-active nanodrugs to rewire macrophages phenotype

Thursday, 15th January - 16:20: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 309

Claudia Codano [1], ***Giuseppe Battaglia*** [1]

1. *Institute for Bioengineering of Catalonia (IBEC)*

Macrophages play a crucial role in regulating immune responses, and their polarisation into M1 ("pro-inflammatory") or M2 ("pro-resolving") phenotypes can have profound effects on inflammatory diseases such as cancer, autoimmune disorders, and chronic infections. When activated, macrophages undergo metabolic rewiring, which drive the release of specific cytokines, such as IL-1β and type I IFNs through accumulation of immunomodulatory metabolites. Current strategies exploit metabolic reprogramming to modulate macrophage function and the release of such inflammatory mediators. However, such strategies lack precision in modulating macrophage behaviour in a controlled and sustained manner. Our goal is to suppress inflammation by leveraging the anti-inflammatory properties of fumarate derivatives combined with selective targeting of macrophages using PPF-PMPC nano-assemblies.

PPF is synthesised by step-growth polymerisation, followed by the addition of PMPC using RAFT polymerisation. The resulting copolymer is analysed by NMR to ensure quality and conversion efficiency. PMPC-PPF NPs are prepared by solvent-switching, and their size and morphology are characterised using DLS and TEM.

Initial studies on THP-1-derived macrophages showed that treatment with PMPC-PPF NPs led to a decrease in TNF-α expression, a pro-inflammatory cytokine, and an increase in IL-10 expression, an anti-inflammatory cytokine. These findings were validated in mouse BMDMs to exclude interference from tumor-associated factors present in THP-1 cells. In BMDMs, treatment with PMPC-PPF NPs similarly reduced pro-inflammatory markers (TNF-α, iNOS) and increased anti-inflammatory markers (Arg1, IL-10) expression in LPS-stimulated macrophages. These effects were further validated by measuring the release of TNF-α and NO, which were both reduced compared to untreated cells.

To investigate the mechanism underlying such anti-inflammatory effects, the activation of the Nrf2 pathway was assessed using HepG2 ARE+ cells, which are modified to express luciferase upon Nrf2 activation. The results demonstrated a dose-dependent activation of Nrf2 in response to PMPC-PPF NPs. Furthermore, PMPC-PPF NPs were tested in a in vivo model of EAE, demonstrating that EAE mice treated with PMPC-PPF NPs exhibited a significant delay in disease onset compared to the untreated group.

In conclusion, the current work has been focused on exploring how PMPC-PPF NPs administration affects macrophage phenotypes, demonstrating both anti-inflammatory properties and the potential for phenotypic rewiring.

Protein corona engineering for precision nanomedicine

Thursday, 15th January - 16:36: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 231

Erica Quagliarini [1]***, Luca Digiacomo*** [1]***, Serena Renzi*** [1]***, Francesca Giulimondi*** [1]***, Daniela Pozzi*** [1]***, Giulio Caracciolo*** [1]

1. *University Sapienza of Rome*

The formation of a biomolecular corona around nanoparticles upon contact with biological fluids critically defines their biological identity and behaviour *in vivo*. Understanding and controlling this phenomenon has become essential for advancing the design of nanomaterials with predictable therapeutic and diagnostic performance (**Figure 1**).

In the therapeutic field, recent studies have focused on optimizing lipid nanoparticles for nucleic acid delivery through a rational combination of microfluidic synthesis, biophysical characterization, and corona engineering. The modulation of the nanoparticle surface composition and the controlled formation of a biomolecular corona have proven to significantly influence cellular uptake, transfection efficiency, and immune recognition. Emerging strategies, such as DNA-mediated surface stabilization, provide an alternative to conventional PEGylation approaches, allowing the development of stealth nanocarriers with enhanced stability and reduced immunogenicity [1,2].

In the diagnostic context, the protein corona has been exploited as a source of disease-specific molecular information. The personalized protein corona, obtained after nanoparticle exposure to human plasma, acts as a molecular fingerprint that reflects individual pathological states. Pattern analysis of corona-associated proteins, through electrophoretic or spectroscopic profiling, has enabled the discrimination of different disease conditions, including various stages of tumor progression[3, 4]. When combined with clinical metadata and statistical modeling, these approaches demonstrate the potential of corona-based assays for early, minimally invasive diagnostics.

Collectively, our findings illustrate how the corona can be transformed from an unpredictable variable into a design parameter for the development of next-generation theranostic platforms [5].

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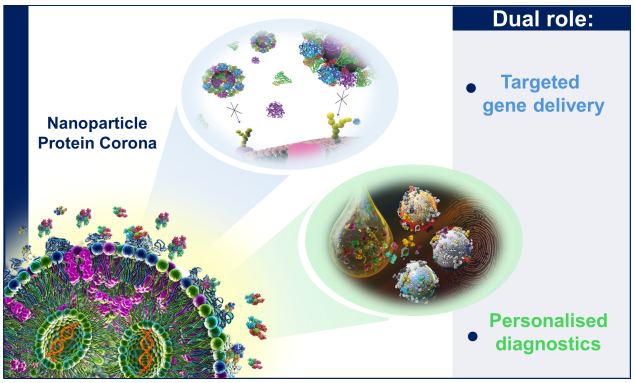
Dual role:
Targeted gene delivery
Nanoparticle Protein Corona
Personalised diagnostics

Figure.png

Theranostic NanoGhosts: Paving the Way from the Bench to the Clinic

Thursday, 15th January - 16:52: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 163

Marcelle Machluf [1]

1. *Technion Israel Institute of Technology*

Effective and targeted delivery remains one of the major challenges in drug delivery and particularely in RNA and gene-based therapeutics. *NanoGhost* is an innovative nano-delivery platform derived from the whole membrane of mesenchymal stem cells (MSCs), designed to combine the intrinsic tumor-homing and immunomodulatory properties of stem cells with a scalable, off-the-shelf nano-vesicle formulation.NanoGhost vesicles preserve key membrane proteins from parental MSCs, enabling selective targeting of pathological tissues, including tumors and inflamed microenvironments. The platform is engineered to encapsulate a variety of small molecules peptides, RNA cargo (e.g., siRNA, mRNA, microRNA) as well as gene-editing tools (e.g., CRISPR-Cas systems), ensuring efficient intracellular delivery with minimal off-target effects.We demonstrate that NanoGhost achieves high stability, biocompatibility, and loading efficiency, while bypassing common limitations of viral vectors and synthetic nanoparticles as well as bypasing the blood brein berriers. Preclinical studies show successful delivery of theraputics leading to GBM inhibition as well as RNA payloads delivery to other tumor sites in vivo. Unpublished data demonstrate that NGs can envelop LNPs thus adding to LNPs the inhernt taegeting ability of MSC to tumors opening the door for a safer nontoxic high loading capacity to the new biohybrid particles.

Intracellular proteins targeting with bi-functionalized magnetic nanoparticles following their endosomal escape

Thursday, 15th January - 17:08: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 239

Mélody Perret [1], Estelle Pineda [1], Mathilde Le Jeune [1], Tieu Ngoc Nguyen [1], Aude Michel [1], Françoise Illien [2], Jean-Michel Siaugue [1], Christine Ménager [1], Fabienne Burlina [2], Emilie Secret [1]

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The activation of cellular processes with magnetic nanoparticles (MNPs) is an emergent topic [1]. However, because of their cellular internalization through endocytosis, MNPs were not able to target intracellular proteins that could be activated to trigger cellular pathways.

Here we will present a strategy that relies on the original bi-functionalization of MNPs with poly(histidine) peptides (PPH), allowing the endosomal escape of the MNPs through proton sponge effect [2], and antibodies, allowing for the first time the targeting of specific proteins once MNPs are in the cytosol. In order to do that, $\gamma Fe_2O_3@SiO_2$ MNPs with diameter smaller than 50 nm, were functionalized with zwitterionic moieties as well as with thiol groups at their surface. These SH groups were used to functionalize them with PPH through a labile link. This labile link between the peptide and the MNPs allows the peptide to be detached from the surface of the MNPs once in the cytosol, in order to avoid any interaction between these peptides and intracellular components, which could hinder the MNPs' intracellular mobility. A second functionalization of the MNPs with targeting antibodies through a non-labile link was then performed, so the MNPs can target specific intracellular proteins once the cytosol has been reached. In a first demonstration of this concept, 89% of MNPs functionalized with both PPH and anti-HSP27 antibodies were able to target intracellular HSP27 [3], after a simple incubation of MNPs with SH-SY5Y cells.

The activation of HSP27, a thermo sensitive protein strongly involved in neuronal differentiation and neurite growth, by localized magnetic hyperthermia is currently studied.

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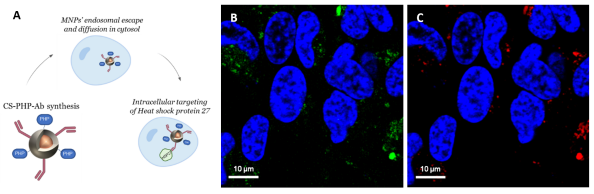

Figure 1. (**A**) Magnetic core-shell nanoparticles bi-functionalized with polyhistidines peptide and anti-HSP27 antibody (CS-PHP-Ab) bypassing endosomal entrapment to reach intracellular thermosensitive proteins HSP27. (**B-C**): Confocal microscopy images on SH-SY5Y cell line, observed 24 h after incubation of CS-PHP-Ab. (**B**) HSP27s appear in green and (**C**) MNPs in red. After particles' endosomal escape, 89 % of MNPs were colocalized with the protein of interest. Cell nuclei are in blue (Hoechst dye 33342).

Image abstract csphpab.png

Engineering sugar-based nanoparticles for delivery of biotherapeutics

Thursday, 15th January - 17:24: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 123

Soraia Fernandes [1], Sukhvir Kaur Bhangu [2], Rong Xu [3], Christoph Hagemeyer [3], Frank Caruso [2], Francesca Cavalieri [2]

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Glycogen is a unique biological dendrimer-like nanoparticle fabricated by nature itself through a bottom-up approach. It is inherently biodegradable, non-toxic, non-immunogenic and can be engineered to possess multi-functional properties. Recently, there has been growing interest in glycogen as a natural alternative to synthetic polymers and nanoparticles in a range of biomedical applications[1]. Herein, we present the engineering of a set of glycogen nanoparticles with tunable sizes (20–80 nm) and surface charges (neutral, negatively and positively charged) designed to serve as (i) an innovative platform for glucose-responsive insulin-delivery[2], (ii) nanocarriers for the delivery of mRNA and small hydrophobic drugs to human T cells and HIV-1 latently infected T cells[3], and (iii) nanocarriers for lymph node-targeted delivery of diverse cargos, including mRNA and antibodies. Remarkably, a single subcutaneous injection of engineered glycogen nanoparticles elicits a rapid and efficient response to glucose challenge in two distinct diabetic mouse models, maintaining optimal blood glucose levels for up to 72 h. Antibody-free glycogen nanoparticles engage T cells and enable successful delivery of mRNA in difficult-to-transfect primary human T cells. Furthermore, our studies demonstrate that glycogen transport within lymph nodes, cellular interactions, and mRNA delivery efficiency are governed by electrostatic interactions and size-exclusion effects. Super resolution microscopy was employed to elucidate the in vivo cellular, subcellular and organ biodistribution of glycogen-based constructs with nanoscale resolution. Our findings highlight the potential of glycogen as a versatile and safe platform for the delivery of a wide range of therapeutics without inducing immune cell activation and cytotoxic effects (Figure 1).

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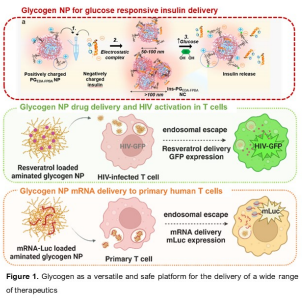

Figure 1. Glycogen as a versatile and safe platform for the delivery of a wide range of therapeutics

Figure 1.jpg

Smart Porous Materials for Precision Therapy

Thursday, 15th January - 17:40: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 95

Ali Trabolsi [1]

1. *New York University Abu Dhabi*

The development of multifunctional drug delivery systems (MDDS) arose from the need to overcome drug-related limitations such as cytotoxicity, immunogenicity, short circulation times, and lack of targeting. Advances in nanobiotechnology have enabled MDDS to serve dual purposes: therapy and diagnostics, via single platforms capable of bioimaging and enhanced therapeutic efficacy. These systems often utilize stimuli-responsive nanostructures that react to biological cues—such as pH, temperature, redox conditions, reactive oxygen species (ROS), and enzymes—enabling controlled and site-specific drug release. This paradigm in nanomedicine has broad applications in cancer therapy, tissue engineering, and bionics, using the intrinsic properties of nanoparticles for theranostic (therapy + diagnostic) functionalities.

The Trabolsi group has developed a series of covalent organic frameworks (COFs) as smart, trigger-responsive MDDS for applications ranging from cancer treatment and bioimaging to diabetes management. Nanoscale COFs exhibit large surface areas, tunable pore geometries, crystallinity, and physiological responsiveness—making them promising nanomedicine platforms. Their ordered porous structure allows efficient drug or protein loading and controlled release. Furthermore, their modular design provides exceptional versatility and environmental responsiveness.

Recently, we reported the synthesis of an imine-linked COF for cancer therapy, which remained stable in physiological conditions but degraded in acidic environments—ideal for targeting solid tumors with site-specific drug release. In another study, by modifying the linkers, we created a triazine-based COF with stability in harsh acidic conditions suitable for oral insulin delivery. In vivo experiments on diabetic rats showed that the insulin-loaded COF successfully crossed the intestinal barrier and sustained blood glucose reduction to normal levels, without causing systemic toxicity.

Through this research, we aim to answer a central question: *Can COF nanoparticles serve as effective therapeutic agents across multiple diseases?* Our findings so far indicate that with smart design and stimuli-responsiveness, COFs represent a promising frontier in the future of targeted and personalized medicine.

CD44-targeted PLGA-based nanoparticles for the delivery of siRNA to cancer cells

Thursday, 15th January - 16:20: Novel Delivery Strategies (Room 1) - Oral - Abstract ID: 218

Pasquale D'Anna [1], Virgilio Piccolo [2], Simona Laurino [3], Sabino Russi [4], Fabio Salvatore Palumbo [5], Geppino Falco [6], Salvatore Emanuele Drago [5], Gennara Cavallaro [5], Cameron Alexander [7], Fabiana Quaglia [1], Claudia Conte [1]

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Polymeric nanoparticles (NPs) are attractive candidates for the delivery of siRNA, alone or in combination with conventional anticancer drugs (1). In order to improve NP accumulation in solid tumors, it is recognized that Hyaluronic Acid (HA) is an important targeting ligand that promotes the cellular uptake of NPs by CD44-presenting cancer cells (2). In this scenario, here, we propose novel CD44-targeted NPs modified on the surface with HA intended for siRNA delivery to solid tumors.

Different HA-coated poly (D, L-lactide-co-glycolide) (PLGA) NPs with or without a poly(ethylene glycol) sheddable surface were prepared through nanoprecipitation or emulsion/diffusion technique, depending on the type of PLGA as well as the cationic moiety employed for siRNA complexation and delivery (Polyethylenimine, protamine, or DOTAP). Hydrodynamic diameter, polydispersity index, and zeta potential of the NPs were measured on a Zetasizer Nano ZS (Malvern Instruments Ltd, Malvern, UK). NPs showed a size below 200 nm with a PI of 0.1 and a negative zeta potential, compatible with an i.v. administration. The loading of siRNA was determined by RiboGreen assay and agarose gel electrophoresis, revealing that siRNA was loaded inside NPs at different N/P ratios depending on the cationic agent added into the formulations. To obtain a NP powder with long-term stability, we conducted freeze-drying studies using various cryoprotectants, including sucrose, trehalose, and hydroxypropyl β-cyclodextrin (HPβCD). The most promising results were obtained with HPβCD. In fact, after lyophilization and NP dispersion in simulated biological media, the colloidal properties of NPs did not change significantly. Subsequently, cytotoxicity, cellular uptake, and transfection studies were performed in different cancer cell lines, which overexpress the CD44 receptor (colon, breast, and gastric cancer cells). NPs demonstrated excellent biocompatibility, high cellular internalization driven by the CD44 receptor, and effective gene silencing capability.

With the aim to overcome MDR, further studies based on the co-entrapment of a therapeutic siRNA combined with a conventional anticancer compound are ongoing.

Acknowledgements

We acknowledge the "My First AIRC grant 2023" (29369).

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Redox-responsive PEGylated sheddable nanoparticles for the delivery of siRNA to cancer cells

Thursday, 15th January - 16:36: Novel Delivery Strategies (Room 1) - Oral - Abstract ID: 216

Virgilio Piccolo [1], ***Annarita Velleca*** [2], ***Simona Laurino*** [3], ***Sabino Russi*** [3], ***Geppino Falco*** [4], ***Fabiana Quaglia*** [2], ***Claudia Conte*** [2]

1. *1 University of Naples Federico II, Department of Pharmacy, Naples,* ***2.*** *University of Naples Federico II, Department of Pharmacy, Naples,* ***3.*** *2IRCCS-CROB, Referral Cancer Center of Basilicata, Rionero in Vulture, Potenza,* ***4.*** *University of Naples, Department of Biology, Naples*

Polymeric nanoparticles (NPs) represent a key technology for the delivery of siRNA to solid tumors[1]. In particular, poly(ethylene glycol) (PEG) coating improves steric stabilisation and prevents immune recognition. Despite these advantages, PEGylation reduces the uptake of NPs from cancer cells. Consequently, a targeting ligand able to encourage cell uptake, such as hyaluronic acid (HA), is often needed[2]. Here, we propose novel HA-targeted NPs intended for siRNA delivery with a redox-responsive linkage able to enter inside cancer cells via the CD44 receptor and lose the PEG coating in the intracellular compartment due to the high redox potential typical of cancer cells.A redox-responsive poly (D, L-lactide-co-glycolide) (PLGA)-ss-PEG block copolymer was synthesised and employed to prepare redox-responsive NPs through an emulsion/solvent diffusion technique. Polyethylenimine (PEI) was added in the organic phase during NP preparation to bind siRNA through electrostatic interactions, whereas HA was added on the NP surface. Spherical NPs of around 100 nm with a low polydispersity index, a negative zeta potential, and a complete entrapment of siRNA were obtained (Fig.1C). FALT studies, the PEG iodine and the Ellman assay were performed at a simulated intracellular level of reducing agents, demonstrating a partial PEG shedding of NPs after 24h of incubation (Fig.1A-B). Unloaded NPs showed long-term stability if freeze-dried in the presence of hydroxypropyl-β-cyclodextrin (HPbCD) as cryoprotectant. NPs were well-tolerated by human red blood cells (RBC) (Fig. 1D) and by a 2D model of GC cells up to a concentration of 0.1 mg/mL and 72h of incubation, thus hiding the intrinsic cytotoxicity of PEI due to the presence of the HA coating (Fig.1E). Uptake studies showed a more pronounced internalisation of HA-coated RR-NPs compared to NPs without HA in CD44+ gastric cancer cells, as clearly evident in CLSM images (Fig.1F) and FACS analysis. Ongoing investigations aim to synthesise novel CD44 targeting peptides and deliver a therapeutic siRNA with a conventional anticancer drug in combination to overcome multidrug resistance (MDR).

Acknowledgements We acknowledge the “My First AIRC grant 2023” (29369).

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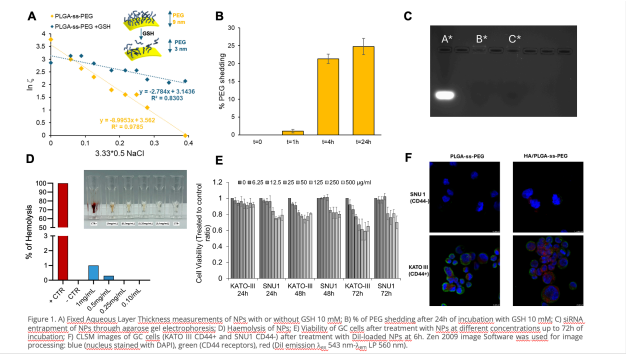

Figure 1. A) Fixed Aqueous Layer Thickness measurements of NPs with or without GSH 10 mM; B) % of PEG shedding after 24h of incubation with GSH 10 mM; C) siRNA entrapment of NPs through agarose gel electrophoresis; D) Haemolysis of NPs; E) Viability of GC cells after treatment with NPs at different concentrations up to 72h of incubation; F) CLSM images of GC cells (KATO III CD44+ and SNU1 CD44-) after treatment with DiI-loaded NPs at 6h. Zen 2009 image Software was used for image processing; blue (nucleus stained with DAPI), green (CD44 receptors), red (DiI emission λ_{ex} 543 nm-λ_{em} LP 560 nm).

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Poly(β-amino ester) based pulmonary siRNA delivery to T-Cells: A Potential Approach for Asthma Therapy

Thursday, 15th January - 16:52: Novel Delivery Strategies (Room 1) - Oral - Abstract ID: 201

Anny Nguyen [1], ***Min Jiang*** [1], ***Joschka T. Müller*** [1], ***Muge Molbay*** [1], ***Simone Carneiro*** [1], ***Adrian Kromer*** [1], ***Felix Sieber-Schäfer*** [1], ***Diana Porras-Gonzalez*** [2], ***Gerald Burgstaller*** [2], ***Bastian Popper*** [3], ***Olivia M. Merkel*** [1]

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Introduction:

Asthma is a complex, heterogeneous respiratory disorder with cytokine-mediated inflammation, particularly in allergic forms. Type 2 T-helper (Th2) cells drive this process by secreting IL-4, IL-5, and IL-13. Targeting GATA3, the transcription factor regulating these cytokines, is a promising therapeutic strategy.[1] However, efficient RNA delivery to T cells remains challenging.[2] To overcome this, we developed Transferrin(Tf)-conjugated Poly(β-amino ester) (PBAE) micelleplexes that enhance siRNA stability and target activated T cells, offering an effective approach for severe asthma (Fig.**1A**).

Methods:

Asthmatic conditions were modeled *ex vivo* by activating T cells in human precision-cut lung slices (PCLS) with CD3/CD28 Dynabeads three days before transfection. GATA3 mRNA was quantified 48 h after siRNA transfection by RT-qPCR. *In vivo*, asthma was induced in female Balb/c mice by Ovalbumin sensitization (days 0, 14) and inhalative challenges (days 24-26, 36-38), with intratracheal micelleplex treatment on days 36-38 (Fig.**1C**). Biodistribution of AF647-siRNA nanoparticles was analyzed by IVIS. Lung CD4+ T-cells were isolated for GATA3 qPCR, total serum IgE was measured by ELISA, and bronchoalveolar cytokines by LEGENDplex ELISA.

Results:

In human PCLS, Tf-PBAE micelleplexes achieved ~60% GATA3 knockdown, surpassing non-conjugated PBAE and identifying it as the lead candidate for *in vivo* studies (Fig.**1B**). Forty-eight hours after the last intratracheal administration, AF647-siRNA fluorescence was mainly detected in lungs and liver for the Tf-PBAE group, whereas free siRNA showed no signal, indicating improved pulmonary retention and protection from degradation (Fig.**1D**). Unprotected siRNA did not reduce GATA3 mRNA *in vivo*, whereas Tf-PBAE micelleplexes led to ~60% knockdown compared to free siRNA (Fig.**1E**). Total serum IgE concentrations declined by ~25%, suggesting reduced systemic IgE (Fig.**1F**). IL-4, IL-5, and IL-13 decreased to near-healthy levels, unlike carrier–control siRNA, indicating a siRNA-specific effect (Fig.**1G**). At this dose, Tf-PBAE siGATA3 caused a slight, non-significant IL-6 increase and significantly reduced TNF-α, indicating no acute inflammation (Fig.**1H**).

Conclusion:

Ex vivo and *in vivo* data demonstrate that Tf-PBAE micelleplexes enable efficient and targeted siGATA3 delivery, resulting in marked GATA3 knockdown and reduced Th2 cytokine and IgE levels, highlighting their potential for asthma therapy.

References:

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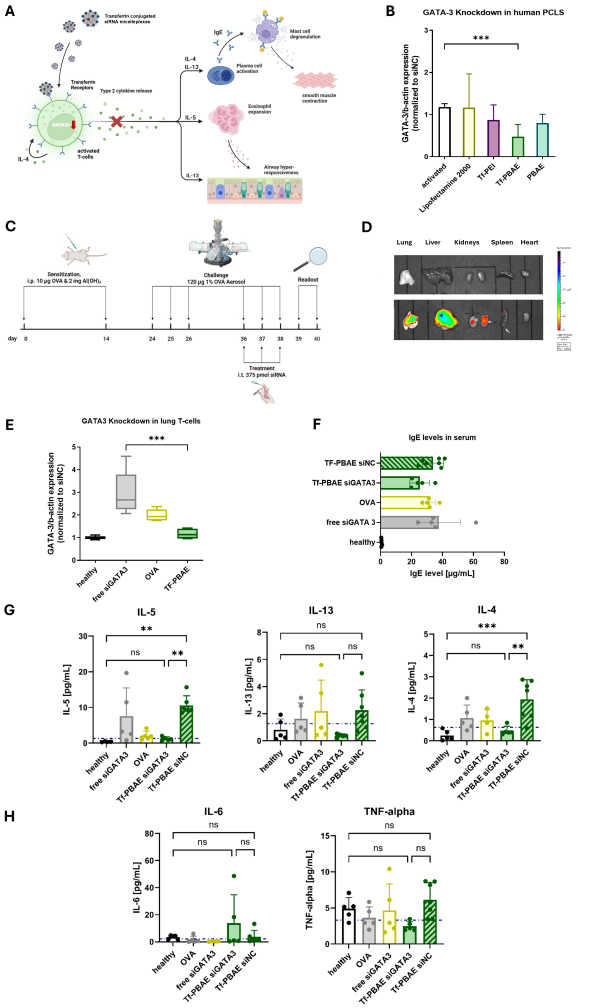

Figure 1| Transferrin-Conjugated PBAE Micelleplexes for siRNA-mediated GATA3 Knockdown. A) Schematic of Blocking GATA3-Th2 Signaling in Type 2 Asthma Using siRNA Transferrin receptor targeted Micelleplexes. **B)** Relative expression of GATA3 in *ex vivo* activated human precision cut lung slices after 48 h incubation. Data are presented as mean ± SD, N = 2; Unpaired t-test, ***P< 0.001. **C)** Overview of *in vivo* study design: Asthma induction and treatment scheme in BALB/c mice. **D)** Biodistribution of free AF647-labeled siRNA (upper) and siRNA encapsulated in Tf-PBAE micelleplexes (lower). **E)** Relative expression of GATA3 in isolated lung T cells 48 h after three consecutive dose administrations. Comparison of **F)** total IgE levels in blood serum and **G)** Type 2 cytokines in bronchoalveolar lung fluid (BALF). **H)** Evaluation of pro-inflammatory effects by quantification of IL-6 and TNF-α levels in BALF. Data are presented as individual animals per datapoint and mean ± SD. Dashed lines indicate assay LOD. A one-way ANOVA was used to determine the significance (**P<0.01,***P<0,001)

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Biomimetic nanoghost lipid nanoparticles for RNA delivery in cancer therapy

Thursday, 15th January - 17:08: Novel Delivery Strategies (Room 1) - Oral - Abstract ID: 129

miriam colombo [1]

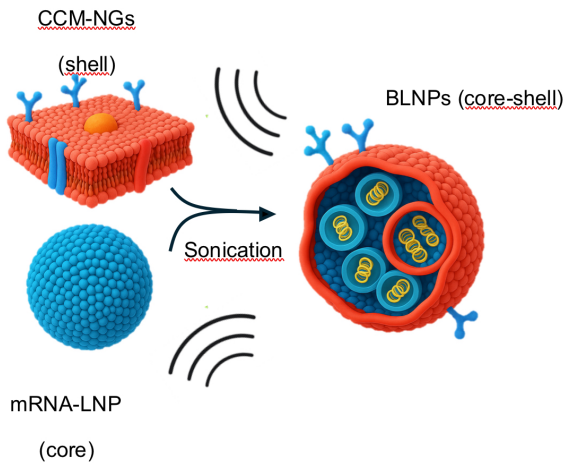
1. *University of Milano-Bicocca*

Lipid nanoparticles (LNPs) are a clinically validated nonviral RNA delivery system, but their limited tumor tropism remains a challenge in oncology. To enhance targeting, LNPs were integrated with cancer cell membrane components, exploiting tumor-derived membranes for homotypic and heterotypic recognition.

A biomimetic nanocarrier was developed by cloaking RNA-loaded LNPs with nanoghosts from 4T1 triple-negative breast cancer cell membranes. These nanoghosts were dye-labeled and characterized for size, charge, protein composition, and membrane orientation. Functionally oriented membrane proteins enabled selective binding to both 4T1 cells and cancer-associated fibroblasts, confirmed by flow cytometry and microscopy.

RNA-LNPs were incorporated into nanoghosts via ultrasound-assisted fusion, yielding stable biomimetic LNPs with a multilamellar mRNA-LNP core and a nanoghost shell. Unlike uncoated LNPs, biomimetic LNPs showed strong uptake by fibroblasts and enhanced internalization and RNA transfection in 4T1 cells, resulting in improved biological activity.

This study demonstrates that RNA-LNPs integrated into biomimetic carriers can achieve dual targeting of tumor and stromal cells, offering a promising strategy to overcome stromal barriers in desmoplastic tumors such as triple-negative breast cancer.



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Ion-dependent protein granules as tunable depots: Applications in vaccination

Thursday, 15th January - 17:24: Novel Delivery Strategies (Room 1) - Oral - Abstract ID: 102

Eloi Parlade [1], ***Marianna Teixeira De Pinho Favaro*** [1], ***Eric Voltà-Durán*** [2], ***Hector Lopez-Laguna*** [3], ***Antonio Villaverde*** [1], ***Esther Vazquez*** [1]

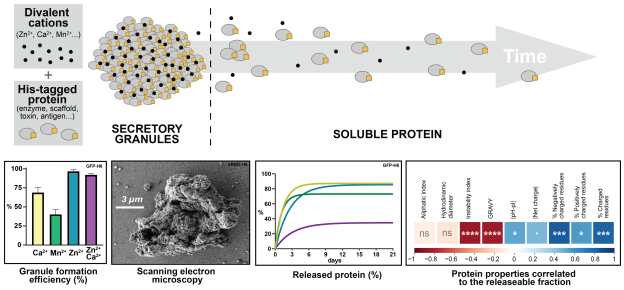
1. *Universitat Autonoma de Barcelona,* ***2.*** *Universitat Politècnica de Catalunya,* ***3.*** *Universitat Internacional de Catalunya*

The sustained delivery of therapeutic proteins remains a major challenge in biomedicine, particularly when aiming for biocompatibility and simplicity of formulation. Inspired by the way endocrine cells store hormones, we developed synthetic protein granules composed exclusively of recombinant proteins and divalent cations, without the need for scaffolds or carriers. By coordinating histidine residues with ions such as Zn^{2+}, Ca^{2+}, Mg^{2+}, or Mn^{2+}, proteins can be packaged into microscale depots that are mechanically stable yet progressively disintegrate under physiological conditions, releasing functional protein over time. Importantly, this strategy is broadly applicable: virtually any protein can be adapted through the introduction of short histidine tags, histidine-rich extensions, or naturally occurring histidine-rich domains.

We investigated precipitation dynamics, release profiles, and in vivo functionality with diverse model proteins. Among the tested ions, Zn^{2+} and Ca^{2+} showed the most desirable outcomes, efficiently assembling proteins into depots while allowing gradual disintegration in physiological conditions. Subsequent work revealed that release dynamics are not governed by the cation alone. Intrinsic protein properties, particularly electrostatic charge and hydropathicity, critically shape granule disintegration and protein availability. Indeed, protein features exerted a stronger impact on release kinetics and the fraction of releasable protein than the choice of cation itself.

While the clinical potential of these granules has been explored with enzymes, scaffolds, and toxins, for vaccine applications we first demonstrated their biosafety and systematically characterized their granulometry and mechanical properties. As a proof-of-concept, we then applied the platform to SARS-CoV-2 immunization. Subcutaneous administration of Zn^{2+}-driven granules containing the Spike receptor-binding domain elicited robust neutralizing antibody responses in mice and significantly reduced disease severity upon viral challenge in golden Syrian hamsters.

This dual demonstration of safety and efficacy highlights the platform's ability to function both as a sustained protein release system and as a self-formulated vaccine depot, without the need for adjuvants. Altogether, ion-driven protein granules offer a versatile and biocompatible strategy for controlled protein delivery, with potential applications ranging from chronic protein replacement to next-generation vaccine design.



Ion-dependent protein granules as tunable depots figure.png

Engineered Red Blood Cells-derived Extracellular Vesicles for combined chemotherapy

Thursday, 15th January - 17:40: Novel Delivery Strategies (Room 1) - Oral - Abstract ID: 233

Miriam Romano [1], Selene Tassoni [1], Angelo Musicò [1], Lucia Paolini [2], Andrea Zendrini [1], Ingrid Cifola [3], Serena Mazzucchelli [4], Giuseppe De Palma [5], Marco Severgnini [3], Fabio Corsi [6], Paolo Bergese [1], Annalisa Radeghieri [1]

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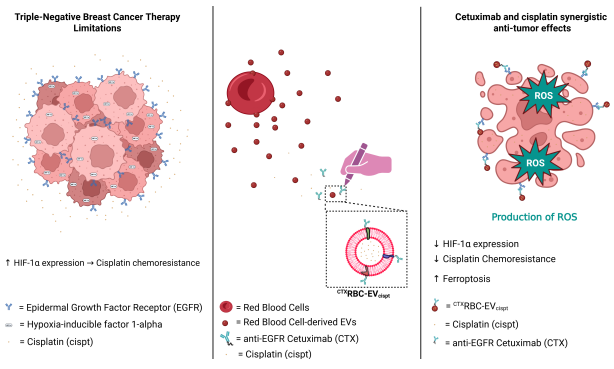
Red blood cell-derived extracellular vesicles (RBCEVs) represent an emerging class of sustainable drug carriers, combining biocompatibility, low immunogenicity, and scalability. Their biogenesis through plasma membrane budding ensures the formation of homogeneous populations with defined physicochemical properties. Importantly, RBCEVs can be produced in large quantities from a patient's own red blood cells, opening for personalized nanomedicine while addressing key challenges of reproducibility, heterogeneity, and, partially, sourcing associated with other biogenic vesicles.

We explored the use of RBCEVs as delivery platforms for the treatment of triple-negative breast cancer. We first focused on engineering vesicle surface with the monoclonal antibody Cetuximab which bears high affinity for Epidermal Growth Factor Receptor, highly expressed in triple-negative breast cancer cells.

Building on this targeting strategy, we designed a synergistic chemotherapeutic nanocarrier by loading Cetuximab-functionalized RBCEVs with cisplatin. This engineered nanocarrier demonstrated enhanced anticancer efficacy in triple-negative breast cancer models, both in vitro and in patient-derived organoids. Mechanistically, the combination increased cisplatin uptake, downregulated hypoxia-related genes, and triggered ferroptosis pathways. Importantly, the nanocarrier also reduced hemotoxicity compared to free drug administration.

Our findings highlight the potential of RBCEVs as a versatile and promising platform for advanced therapeutic applications.



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Optical Nanomaterials as Frequency Converters for Imaging

Friday, 16th January - 09:00: Plenary Session 1 (Auditorium) - Plenary Speaker - Abstract ID: 1

Xiaogang Liu [1]

1. *National University of Singapore*

Imaging technology has revolutionized our understanding of the world, from medical diagnosis to astronomical exploration. Advancements in imaging tools have led to significant breakthroughs across various sectors. The field continually evolves, with technologies like lanthanide doping in optical nanomaterials emerging as a promising research area. This technique aims to improve image resolution and open up new application possibilities. Lanthanides are notable for their specific light absorption and emission capabilities, useful in frequency conversion to change light into new wavelengths. Photon upconversion, a notable research area, converts low-energy photons to higher-energy ones, enhancing imaging, bio-detection, therapy, and X-ray scintillation. I will also discuss recent advancements in electronic assistive technologies for individuals with disabilities, highlighting the transformative potential of these innovations.

Potent biocompatible polymer virucides for preventing future viral outbreaks

Friday, 16th January - 09:40: Plenary Session 1 (Auditorium) - Plenary Speaker - Abstract ID: 316

Samuel Jones [1]

1. *School of Chemistry, University of Birmingham*

TBA

Nearing single vesicle-resolved lipidomics of circulating extracellular vesicles (EVs) to untangle the EV interactome in cancer

Friday, 16th January - 10:50: Plenary Session 2 (Auditorium) - Plenary Speaker - Abstract ID: 314

Randy Carney [1]

1. *University of California, Davis*

TBA

The lipidomic architecture of the mouse brain

Friday, 16th January - 11:30: Plenary Session 2 (Auditorium) - Plenary Speaker - Abstract ID: 156

Giovanni D'Angelo [1]

1. *EPFL*

Lipids are fundamental components of the brain, crucial for synaptic transmission and signal propagation. Altered brain lipid composition is associated with neuropathologies and ageing, yet, the spatial organization of the mammalian brain lipidome remains insufficiently characterized compared to other modalities. Here, we mapped the membrane lipid architecture of the adult mouse brain at micrometric scale, across sexes, and during pregnancy. This Lipid Brain Atlas reveals that lipids define a fine-grained biochemical structure that aligns with functional anatomy. Membrane lipid spatial heterogeneity clusters into territories, which we termed *lipizones*. *Lipizones* partially mirror cell type territories, but also capture distal axon terminals. Through *lipizones,* (i) we reveal new organizing principles for the gray matter related to connectivity, cytoarchitecture, and development; (ii) we discover a new axis of oligodendrocyte heterogeneity in the white matter; (iii) and we find biochemical zonation in the choroid plexus and in the ventricular walls. We show that this lipidomic architecture can adapt to changing physiological needs. In the brain of pregnant females, the white matter is metabolically activated and the outer cortex is reorganized. These results are a foundational resource, poised to reshape our understanding of lipids in brain development, physiology, and pathology.

Ultrasound Mediated Mechanical Thrombolysis Of Blood Clots Using Multi-cavity PLGA Particles

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 11

Srivatsava Sunku [1]

1. *Singhealth*

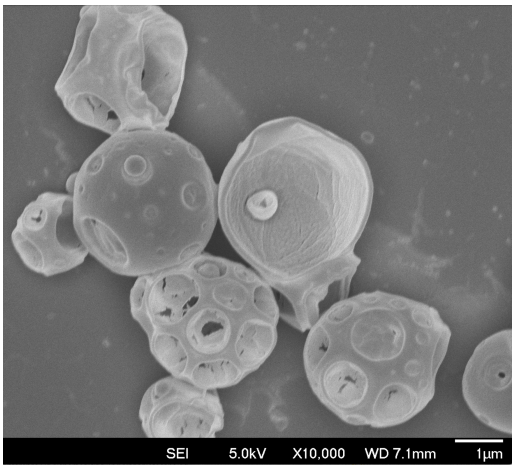
Introduction: Acute vascular thrombi pose significant health risks, and current systemic anticoagulant treatments carry a high risk of hemorrhagic complications. Localised thrombolysis using nano/microscopic phenomena offers a promising alternative.

Objective: This study investigates the feasibility of using Multi-cavity Poly (lactic-co-glycolic acid) Microparticles (mcPLGA-MC) to induce localised mechanical thrombolysis through cavitation when exposed to High-Intensity Focused Ultrasound (HIFU).

Methods: We explored various cavitation agents and subsequently focused on mcPLGA-MCs. These microparticles, with entrapped air pockets, were hypothesised to generate sufficient force upon cavitation to lyse blood clots. An *in-vitro* circulatory model was developed to assess the thrombolytic efficacy of mcPLGA-MCs under HIFU exposure. Clot volume reduction was quantified through direct visualisation and image analysis software. Diagnostic ultrasound imaging was also employed to monitor the microparticles within the model, leveraging their ultrasound contrast properties.

Results: Exposure of mcPLGA-MCs to HIFU successfully induced stable and inertial cavitation. This cavitation effect led to a directly observable and quantifiable reduction in blood clot volume within the *in-vitro* model, confirming mechanical lysis. The ultrasound contrast provided by the micro-particles facilitated real-time monitoring.

Conclusion: Multi-cavity PLGA micro-particles demonstrate significant potential for localised, cavitation-mediated thrombolysis. This approach could minimise the need for systemic anticoagulants and reduce associated complications. Further investigation into the clinical translation of this technology is warranted.



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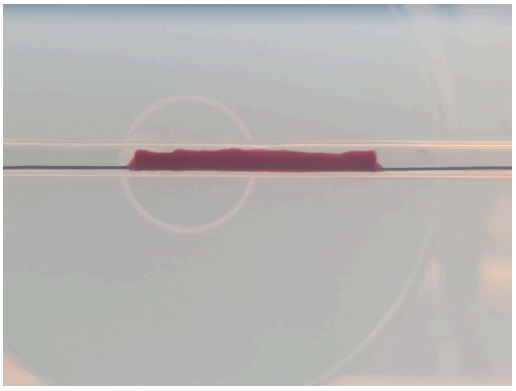
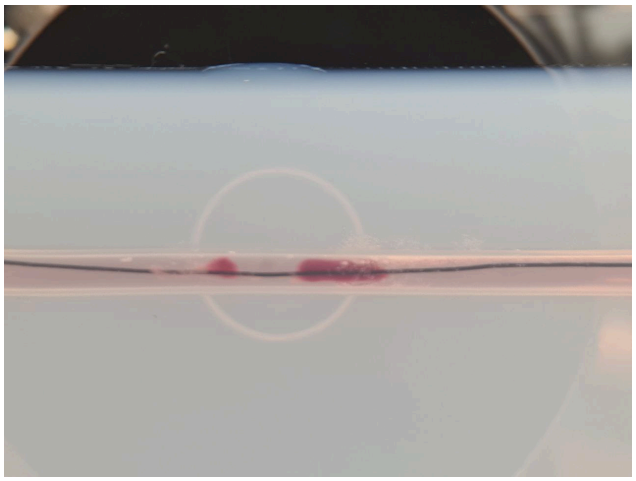


Initial blood clot - pre-thrombolysis.jpeg



Blood clot - final.jpeg

Green-Sourced PHB-HHx for the Design of Docetaxel-Loaded Polymeric Nanoparticles

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 36

Ovidio Catanzano [1], ***Michele Guida*** [2], ***Simona Varriale*** [3], ***Elisabetta Borselleca*** [3], ***Giovanni Dal Poggetto*** [1], ***Fabiana Quaglia*** [4], ***Claudia Conte*** [4], ***Cinzia Pezzella*** [2]

1. *Institute for Polymers, Composites and Biomaterials (IPCB-CNR),* ***2.*** *University of Napoli Federico II,* ***3.*** *University of Napoli Federico II, Department of Chemical Sciences,* ***4.*** *University of Naples Federico II, Department of Pharmacy, Naples*

Breast cancer remains one of the leading causes of cancer-related mortality among women worldwide, and the clinical use of docetaxel is limited by poor solubility, systemic toxicity, and non-specific biodistribution (1). Poly(3-Hydroxybutyrate-co-3-Hydroxyhexanoate) (PHB-HHx) is a natural polyester increasingly explored in biomedicine as a sustainable alternative to petroleum-based polymers for controlled drug delivery (2). In this work, polymeric nanoparticles (NPs) were prepared from PHB-HHx derived from cardoon (*Cynara Cardunculus*) biomass as a sustainable nanocarrier for docetaxel delivery.

PHB-HHx was produced by an engineered *E. coli* strain through the fermentation of glucose derived from cardoon root biomass via green methodologies. The fermentation process was highly efficient, resulting in the accumulation of approximately 30% PHB-HHx within the cells, with an HHx molar fraction of 35%, as determined by H-NMR. GPC analysis revealed that the Mn and Mw of the PHB-HHx were 98.6 kDa and 141.9 kDa, respectively, while DSC analysis confirmed its partial crystalline nature.

Drug-loaded PHB-HHx NPs were prepared via a nanoprecipitation process, resulting in spherical particles with an average diameter of ~200 nm, a polydispersity index below 0.2, and a negative ζ-potential. Particle size and distribution were influenced by polymer concentration and nanoprecipitation parameters, allowing fine-tuning of the formulation to achieve optimal colloidal stability and drug loading efficiency. The NPs exhibited high encapsulation efficiency, demonstrating the strong affinity of the PHB-HHx matrix for hydrophobic compounds. These findings demonstrate that cardoon root biomass represents an effective renewable carbon source for PHB-HHx production. Furthermore, PHB-HHx NPs provide an eco-sustainable and efficient platform for docetaxel delivery, offering a promising strategy to enhance therapeutic performance in breast cancer treatment. Preliminary cytotoxicity studies are ongoing to further evaluate their biocompatibility and anticancer potential.

This research was funded by European Union-Next generation EU, in the frame of PRIN 2022 “BRAIN” project (A Biomass-derived mateRial plAtform for braIn delivery of bioactive compouNds).

1. *Panthi VK, et al.* Journal of Drug Delivery Science and Technology. 2024;92:105314.

2. *Prakash P, et al.* Nanomaterials. 2022;12(1):175.

Iron based nanoparticles for enhanced dual-mode hyperthermia in metastatic melanoma treatment

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 40

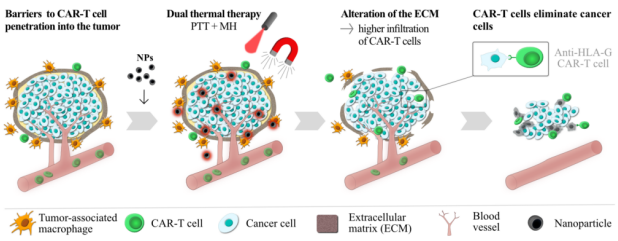
Lorenzo Riccio [1], ***Chiara Puccinelli*** [1], ***Laura Maggini*** [1], ***Davide Bonifazi*** [1]

1. *University of Vienna, Faculty of Chemistry*

Metastatic melanoma remains one of the most worrisome cancers, being the fastest growing malignancy in men and second in women, with an 84% mortality rate after 5 years. Despite recent advances, traditional therapies such as surgery, chemotherapy, targeted therapy and radiotherapy often cause side effects without significantly improving long-term survival. Among novel approaches, immunotherapy and specifically chimeric antigen receptor (CAR) T-cells therapy showed great potential. CAR-T cells are genetically engineered T lymphocytes designed to express chimeric antigen receptors, which allow them to recognize and bind to specific antigens on tumor cell surfaces. Although highly effective in hematological malignancies, CAR-T cell therapy faces substantial challenges in solid tumors such as physical barriers and immunosuppressive tumor microenvironment (TME), which limit CAR-T cell infiltration and effectiveness.

To address these limitations, nanoparticle mediated hyperthermia has emerged as a strategy to disrupt the extracellular matrix of the tumor and enhance CAR-T cell penetration. In this context, iron carbide nanoparticles are particularly attractive due to their ability to generate heat by both magnetic (potentially superior saturation magnetization compared to iron oxide nanoparticles) and optical (higher photothermal conversion efficiency of gold nanorods) hyperthermia. However, iron carbide nanoparticles are not stable in biological environments, and can undergo degradation, releasing iron ions that can be toxic for the organism.

This study investigates the synthesis of Fe_5C_2 and the first reported graphite-like coated Fe_7C_3 nanoparticles. Phase purity was confirmed by X-ray diffraction and the morphology extensively studied using high resolution electron microscopy (HRTEM). Their magnetic properties and corresponding heating under alternating magnetic fields and near-infrared (NIR) irradiation were evaluated using superconducting quantum interference devices (SQUID) magnetometry, vibrating sample magnetometry (VSM) and laser exposure. Furthermore, to address stability and biocompatibility challenges, different coating and functionalization strategies such as polydopamine, phospholipids, gold and diazonium salts were investigated and characterized using techniques including TEM, XRD, thermogravimetric analysis (TGA) and X-ray photoelectron spectroscopy (XPS). Finally, the effect of the coatings on the photothermal performances of the nanoparticles has been evaluated.



Mechanism of action of iron carbide nanoparticles.png

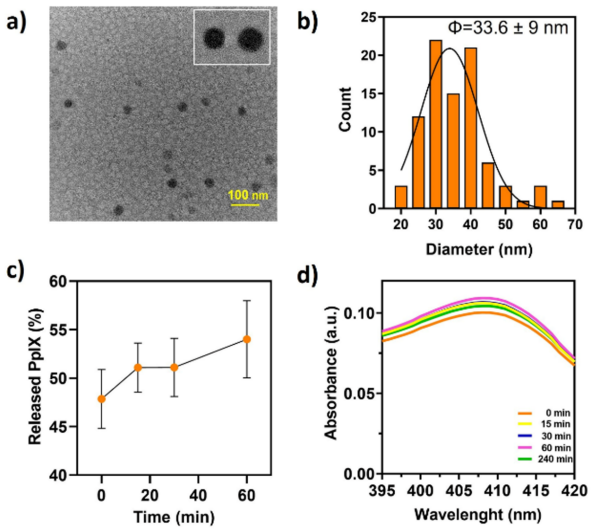
Antimicrobial Photodynamic Therapy Using Encapsulated Protoporphyrin IX for the Treatment of Bacterial Pathogens

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 52

NATALIA IZQUIERDO [1], ***Gracia Mendoza*** [1], ***Manuel Arruebo*** [2], ***Enrique Gámez*** [3], ***Teresa Alejo*** [3]

1. *Aragon Health Research Institute (IIS Aragon), 50009-Zaragoza, Spain.,* ***2.*** *Department of Chemical and Environmental Engineering, University of Zaragoza, Campus Río Ebro-Edificio I+D, C/Poeta Mariano Esquillor S/N, 50018 Zaragoza, Spain,* ***3.*** *Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, Zaragoza 50009, Spain*

Introduction: Antimicrobial Photodynamic Therapy (APDT) uses light-activated photosensitizers to produce ROS and inactivate pathogens [1]. Despite its precision, APDT is limited by poor tissue penetration and photobleaching [2][3]. Encapsulating photosensitizers in nanoparticles can improve efficacy. This study evaluates the antimicrobial effect of free and PLGA-encapsulated protoporphyrin IX (PpIX) against *Staphylococcus aureus*. **Methods:** ROS production by ICG and PpIX was evaluated using the DHR123 probe after laser irradiation (808 nm for ICG, 532 nm for PpIX). Control tests confirmed that ROS generation was light-dependent, not thermal. Photobleaching was assessed via UV-Vis spectroscopy before and after 5 minutes of irradiation. PpIX-loaded PLGA nanoparticles (PpIX-NPs) were synthesized by emulsification–solvent evaporation and characterized by TEM, NTA, and DLS. Encapsulation efficiency, drug loading, and release in PBS/Tween® 20 were measured by UV-Vis. Antimicrobial activity against Staphylococcus aureus (0.5–10 ppm) was tested post-irradiation. Cytotoxicity in fibroblasts was assessed after 24-hour exposure using a viability assay. **Results:** PpIX, either in free form or encapsulated in nanoparticles (PpIX-NPs), was incubated for 24 hours at concentrations ranging from 0.5 to 2 ppm. Antimicrobial photodynamic activity was evaluated by comparing PpIX with ICG in terms of reactive oxygen species (ROS) generation and photobleaching. PpIX exhibited superior ROS production and photostability, supporting its selection for further development. PLGA-based nanoparticles loaded with PpIX were then prepared, showing a spherical morphology with an average diameter of 33.6 ± 9 nm—slightly larger than empty nanoparticles. Zeta potential values were −11.9 ± 0.6 mV for empty NPs and −12.2 ± 1.0 mV for PpIX-NPs, indicating good colloidal stability. The formulation enabled a rapid release of PpIX, reaching 54 wt% within 1 hour. Encapsulation efficiency was 13.7 ± 1.7 wt%, and drug loading was 0.14 ± 0.09 wt%. Encapsulated PpIX showed no cytotoxicity on fibroblasts (viability >70%), whereas free PpIX induced a significant dose- and time-dependent decrease in cell viability. **Conclusions:** PLGA nanoparticles successfully encapsulate PpIX, improving its photostability and antimicrobial efficacy while minimizing cytotoxicity in mammalian cells compared to the free form.



e)

	Mean diameter (nm)	Hydrodinamic diameter (nm)	ζ-Potential (mV)
Empty NPs	16.9 ± 7.2	116.3 ± 36.7	-11.9 ± 0.6
Loaded NPs	33.6 ± 9	121.5 ± 44.5	-12.2 ± 1

Figure 1. (a) TEM images of PpIX-NPs. (b) Diameter distribution histogram of PpIX-NPs. (c) PpIX release kinetics from the particles over a 1-hour period in a PBS solution containing Tween®20 (2%). (d) Ultraviolet-visible spectrum of PpIX-NPs up to 4-hour period of release kinetics assay at 37°C. (e) Measurement of the diameters and ζ-potential of both empty and loaded NPs. Experiments were performed in triplicate (n=3).

Izquierdo natalia abstract image.png

Biodegradable Enzymatic Nanobots for Crossing the Skin Barrier in Healthy Human Models

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 53

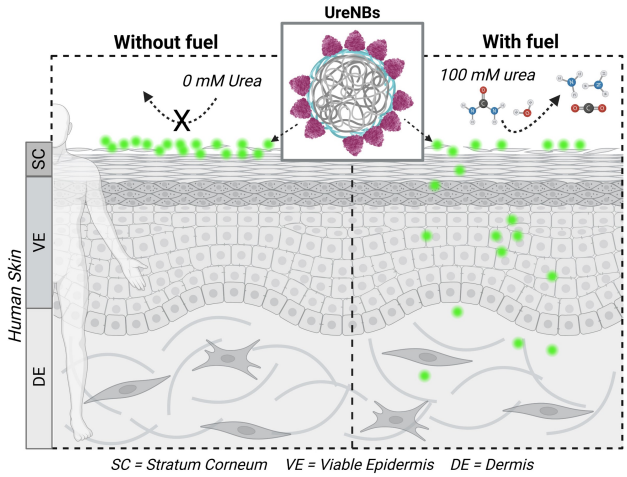
Carles Prado [1], ***Jasper Koning*** [2], ***Taco Waaijman*** [2], ***Inés Macías Tarrío*** [1], ***Cristian Huck*** [3], ***Samuel Sánchez*** [1]

1. *Institute for Bioengineering of Catalonia (IBEC),* ***2.*** *Amsterdam UMC,* ***3.*** *ALBA Synchrotron Light Source*

The skin constitutes the body's primary defensive barrier, a function attributed to its complex and highly dense architecture. Beyond its protective role, the skin represents a promising route for the administration of therapeutics. It offers important advantages over traditional oral and intravenous delivery methods, including the ability to circumvent hepatic first-pass metabolism and eliminate the need for trained personnel and invasive techniques such as needle-based injections. Additionally, it provides a valuable platform for the localized treatment of a wide range of dermatological conditions. However, the bioavailability of topically applied therapeutics is significantly constrained by the architecture of stratum corneum (SC), the outermost layer of the epidermis. Hence, to overcome this barrier, the most widely adopted strategy involves the physical disruption of the SC, which induces adverse effects.

Nanobots (NBs), self-propelled nanoparticles, have recently emerged as next-generation advanced carriers. These types of NBs have demonstrated enhanced drug delivery capabilities in two-dimensional cell cultures, increased cellular uptake, improved diffusion in viscous media, effective penetration of mucosal barriers, and tumor infiltration.

Here, we present an enzymatically powered NB capable of overcoming SC barrier and reaching viable epidermis and dermis more effectively. These NBs were constructed using poly(lactic-co-glycolic acid) (PLGA), an FDA-approved material already used in clinics. Their surface was functionalized with urease, resulting in NBs with a size range of 150-200 nm. To evaluate their skin penetration capabilities, in vitro human skin models were developed using primary cells isolated from donors. Keratinocytes were seeded on top of a dermal matrix composed of collagen and fibroblasts and cultured at an air–liquid interface to promote stratification and differentiation. After three weeks of maturation, NBs in absence and presence of the fuel, were topically applied and incubated on the tissue models. Finally, the models were sliced and imaged to quantify the NBs presence in three distinct skin layers: SC, viable epidermis and dermis.



Picture1.jpg

Evaluation of PLGA/Eudragit® RS100-CuS-ICG Hybrid Nanoparticles for Antimicrobial Photodynamic Therapy in Advanced Skin Infection Models

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 55

Isabel Bescos [1], ***Cristina Quílez*** [2], ***Lucía Abengochea*** [1], ***Pablo Ruiz*** [1], ***Leticia Suárez*** [2], ***Cristina Yus*** [1], ***Manuel Arruebo*** [1], ***Diego Velasco*** [2], ***Víctor Sebastián*** [1]

1. *Department of Chemical and Environmental Engineering, University of Zaragoza, Zaragoza, Spain; Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, Zaragoza, Spain,* ***2.*** *Bioengineering Department, University Carlos III of Madrid, Spain; Fundación Instituto de Investigación Sanitaria de la Fundación Jiménez Díaz, Madrid, Spain*

Multidrug-resistant bacterial infections represent a growing public health challenge, particularly in skin infections [1]. Antimicrobial photodynamic therapy (aPDT) is emerging as a promising alternative, based on the activation of photosensitizers (PSs) by near-infrared (NIR) light to generate reactive oxygen species (ROS) that locally eliminate pathogens [2]. In this work, hybrid nanoparticles (NPs) composed of poly(lactic-co-glycolic acid) (PLGA) and Eudragit® RS100 were developed encapsulating copper sulfide NPs (CuS NPs) and Indocyanine Green (ICG) as PSs. The synthesis was performed using a microfluidic millireactor under continuous flow, allowing precise control over mixing and rendering homogeneous particle size distribution [3]. The resulting NPs showed a size of approximately 150 nm, high colloidal stability, good reproducibility in the amounts of CuS and ICG loading, and strong ROS generation under NIR irradiation. The antimicrobial efficacy was evaluated against *Staphylococcus aureus* ATCC 25923 (*S. aureus*) using two *in vitro* models: a conventional 2D model and an infected 3D model based on a fibrin matrix containing human fibroblasts to mimic the dermis layer, which was further characterized by confocal microscopy. Cytotoxicity was also evaluated in both models. After 5 minutes of NIR exposure, the NPs achieved a 99.8% bacterial reduction in both models (A). Cell viability was higher in the 3D model (84%) compared to 2D (75%), likely due to the protective effect of the fibrin matrix (B). Although temperature increases were observed after NIR irradiation (30 °C in 2D and 15 °C in 3D) (C), the antibacterial effect was confirmed to be exclusively photodynamic, with no significant photothermal contribution. Confocal microscopy revealed that *S. aureus* biofilm formed at the 3D model surface, with limited interaction with cells, which were homogeneously distributed throughout the matrix. Additionally, a more advanced infected 3D skin model with dermal and epidermal layers was used to evaluate the treatment. Initial histological analysis showed a visible reduction in bacterial load following aPDT treatment. These results demonstrate the potential of CuS/ICG-loaded hybrid NPs, synthesized through a scalable continuous-flow platform, as effective PSs for aPDT, and highlight the value of 3D models in the development of innovative nanotechnology-based antimicrobial therapies.

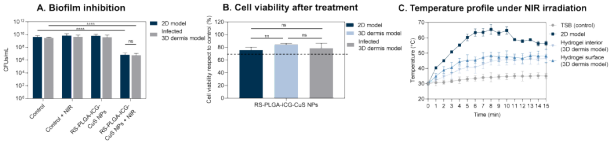


Figure. (A) Biofilm inhibition (CFUs/mL) in the 3D dermis model with and without NIR irradiation. (B) Fibroblast viability in 2D vs. 3D dermis model. (C) Temperature profile of NPs in the 2D and 3D dermis model (interior vs. surface of hydrogel); TSB used as control. ns: not significant; **** = p < 0.0001; ** = p<0,05.

Figure apdt.png

Photoresponsive nanomaterials to prevent bacterial infections on indwelling devices

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 65

Lucia Abengochea [1], ***Cristina Yus*** [1], ***Manuel Arruebo*** [1], ***Víctor Sebastián*** [1]

1. *Department of Chemical and Environmental Engineering, University of Zaragoza, 50018 Zaragoza, Spain; Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, 50009 Zaragoza, Spain*

The development of bacterial biofilms on the surface of indwelling medical devices poses a major clinical risk associated with infection onset, systemic dissemination and, ultimately, device failure (1) – a critical concern, especially in the context of non-replaceable implants. The growing threat of bacterial resistance to conventional antibiotics has intensified the search for safe alternative therapeutic strategies to combat microbial infections. Unlike many chemotherapies or antibiotics that target specific enzymes or proteins, antimicrobial photodynamic therapy (PDT) triggers multiple non-specific mechanisms of animicrobial action, thus hindering the development of bacterial resistances. PDT operates through the light-induced generation of reactive oxygen species (ROS), which have a multitarget effect on bacterial cells by disrupting both their structural components and key metabolic pathways (2).

In this work, biocompatible materials with photo-responsive antimicrobial properties were synthesized as surface coatings for gastrostomy tubes (Gtubes), offering the advantage of an on-demand, light-triggered disinfection that not requires sustained antimicrobial release. Gtubes were cut into 0.5cm wide sections and coated with natural-derived polymeric matrices loaded with indocyanine green (ICG) and CuS nanoparticles. As the first hours are decisive in bacterial colonization of implants, the coated Gtube sections were incubated for 3h with GFP-expressing *Staphylococcus aureus,* in order to evaluate the effect of the coatings on the inhibition of biofilm formation. Upon 808 nm near infrared (NIR) exposure, the top-performing nanocoating showed a robust antimicrobial response, reducing bacterial viability by more than 99%, in contrast to the non-irradiated, identically coated samples. These findings underscore the potential of PDT as an effective strategy for localized disinfection in indwelling medical devices and highlight the broader applicability of the coating to other surfaces where light-activated antibacterial control may be advantageous.

(1) Rodrigues LR. *Inhibition of bacterial adhesion on medical devices*. Adv Exp Med Biol. 2011;715:351–67.

(2) Hu X, et al. *Antimicrobial Photodynamic Therapy to Control Clinically Relevant Biofilm Infections*. Front Microbiol. 2018;9:1299.

Funding for this research was provided by the Spanish Ministry of Science and Innovation and Universities (grant numbers PID2021-127847OB-I00 and PID2023-146091OB-I00).

Modular Functionalisation of Anisotropic Antimicrobial Nanoparticles for Combating Antimicrobial Resistance

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 92

Heba Elgamodi [1], ***Zeljka Krpetic*** [1], ***Rosa Arrigo*** [1]

1. *School of Science Engineering and Environment, University of Salford, United Kingdom*

Antibiotic resistance has been recognised by the World Health Organization (WHO) as one of the most critical global health threats of the twenty-first century. According to the Global Antibiotic Research and Development Partnership (GARDP), an estimated 700,000 individuals die annually from infections caused by drug-resistant pathogens. Without urgent and coordinated action, these figures are projected to escalate, threatening the effectiveness of modern medicine and public health systems worldwide. Consequently, there is an urgent need to accelerate research into innovative therapeutic approaches and the development of novel antimicrobial agents capable of addressing the growing challenges of antimicrobial resistance.

Here we report a systematic study engaging a modular approach to particle synthesis and surface functionalisation, aimed at understanding the role of particle shape and surface chemistry functionalisation on the antimicrobial effects of copper-based anisotropic nanoparticles against clinically significant resistant pathogens (*Pseudomonas Aeruginosa* band *Staphylococcus Aureus*). This interdisciplinary research focuses on the design and development of novel protocols for assessment of the library of copper-based nanoparticles. Moreover, we present and characterize the effects of relevant biological media on the stability of engineered functional nanoparticles *in situ* profiling the formation of biomolecular coronas and further investigate their cytotoxicity prior to advancing steps towards therapeutic applications.

Recognising the constraints of traditional microbiological assays for evaluating the antimicrobial activity of functional nanomaterials *in vitro*, this work proposes the implementation of novel, robust protocols specifically designed for engineered functional plasmonic nanoparticle systems. By systematically addressing both the opportunities and challenges associated with application of copper-based nanomaterials, this work advances the field of antimicrobial nanomedicine and highlights the importance of nanoparticle design and characterisation strategies. We anticipate that our findings will contribute to the rational design strategies of next-generation nanoparticle-based plasmonic therapeutics and support global efforts to mitigate the escalating threat posed by AMR.

Comparative evaluation of nanoemulsion and mesoporous silica nanoparticles as delivery systems for Tasmannia lanceolata and Backhousia citriodora essential oils against dental caries pathogen

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 106

Ratih Pusporini [1], ***Maral Seididamyeh*** [1], ***Anh Dao Thi Phan*** [1], ***Chun Xu*** [2], ***Run Zhang*** [1], ***Yasmina Sultanbawa*** [1]

1. *The University of Queensland,* ***2.*** *The University of Sydney*

The increasing prevalence of dental caries and antimicrobial resistance among oral pathogens highlights the need for novel therapeutic strategies. Essential oils (EOs) derived from *Tasmannia lanceolata* and *Backhousia citriodora* exhibit strong antimicrobial properties; however, their clinical potential is hindered by volatility, low aqueous solubility, and instability. This study aims to develop and compare two nanocarrier-based delivery systems—nanoemulsions (NEs) and mesoporous silica nanoparticles (MSNs)—to enhance the bioavailability and efficacy of these EOs. Currently, formulation and synthesis of both systems are underway. Physicochemical characterization will be performed using dynamic light scattering (DLS) for particle size and zeta potential, transmission electron microscopy (TEM) for morphological analysis, and Fourier-transform infrared spectroscopy (FTIR) to confirm encapsulation and chemical interactions. Subsequent in vitro assays will evaluate and compare the antimicrobial and antibiofilm activities of the EO-loaded NEs and MSNs against key cariogenic pathogens, including *Streptococcus mutans* and *Candida albicans*. The outcomes are expected to provide insight into the suitability of each delivery system for oral health applications. Final experimental results are currently being generated and will be presented on the day of the presentation

From charge density tuning to delivery: Diisopropylaminoethyl-functionalized chitosan as a versatile siRNA vector

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 124

Marcio Tiera [1], ***André Martinez Júnior*** [1], ***Thalles Ruiz*** [1], ***Patricia Vilamaior*** [1], ***Vera Oliveira Tiera*** [1], ***Sebastião Taboga*** [1]

1. *São Paulo State University (UNESP), São José do Rio Preto*

Chitosan and its derivatives have been widely studied as non-viral vectors for gene therapy due to properties such as low cytotoxicity and biodegradability. However, their nanoparticles show low stability at neutral pH and poor delivery into target cells. To overcome these drawbacks, the charge density of the polymer backbone was tuned by gradually introducing diisopropylaminoethyl (DIPEA) groups and short PEG chains via bioreducible disulfide linkages.

A series of chitosan derivatives substituted with DIPEA (DDIPEA) and PEG groups were synthesized and characterized, aiming to control charge density and nanoparticle behavior at neutral pH. All substituted polymers were lysozyme-degradable and showed low cytotoxicity across HeLa-GFP, RAW 264.7, HaCaT, and NIH/3T3 cells. Nanoparticles (150–200 nm) loaded with siRNA-TNF or siRNA-GFP were obtained by coacervation at neutral pH and maintained high cell viability (>80%). A clear correlation emerged between charge density and nanoparticle properties such as hydrodynamic diameter (Dh) and zeta potential. In vitro experiments demonstrated increased gene silencing for more substituted polymers, achieving 65% knockdown of GFP in HeLa cells and 70% silencing of TNFα in stimulated RAW 264.7 macrophages. PEG chains provided additional stability to nanoparticles at pH 7.4 and 150 mM ionic strength. These results emphasize the role of surface charge and stability in transfection efficiency (1).

In vivo, a psoriasis-like skin inflammation Muridae model was treated with the selected vector (56% DIPEA substitution) loaded with siTNFα. Treatment reduced TNFα to levels comparable to those in non-IMQ-treated animals. Reduced expression of F4/80, a glycoprotein abundant in phagocytic cells and major contributor to TNFα production, confirmed therapeutic potential. These findings highlight DIPEA–PEG chitosan derivatives as promising siRNA carriers for inflammatory skin disorders.

This study was financially supported by the São Paulo Research Foundation (**FAPESP**), **grants 2019/27801-0 and 2023/03182-4, CNPq 401811/2024-7.**

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(1) Martinez Junior, A.M., Ruiz, T.F.R., Vilamaior, P.S.L. et al. Topical delivery of siRNA to psoriatic skin model using high molecular weight chitosan derivatives: In vitro and in vivo studies. Drug Deliv. Transl. Res. 15, 3199–3225 (2025)

Gallium-based Drug Nanocarriers for the Treatment of Lung Infections

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 135

Shengtao Yu [1], ***Georgios A. Sotiriou*** [2]

1. *Karolinska Institutet,* ***2.*** *Stockholm University*

Introduction: Antimicrobial resistance (AMR) is a major threat to the global health, prompting new strategies that enhance potency of existing antibiotics. Gallium-based materials have been reported as antibacterial agents due to their similar physicochemical properties to ferric ions (Fe^{3+}), which are essential to nearly all bacteria. As a result, utilizing materials that can release Ga^{3+} can disrupt bacterial iron homeostasis and metabolism. Beyond their intrinsic antimicrobial properties, nanoparticles also have substantial potential as carriers for the delivery of therapeutic agents. Our lab previously demonstrated that calcium phosphate nanoparticles produced by flame spray pyrolysis (FSP) loaded with antimicrobial peptides exhibited potent antibacterial activity. This project aims to investigate the use of gallium-based nanoparticles as drug nanocarriers for the delivery of both antibacterial macromolecules and small molecules and evaluate their synergistic effect of antibacterial efficacy.

Methods: Gallium-based nanocarriers were synthesized via FSP. LL37, human cathelicidin antimicrobial peptide, was selected as the model macromolecule. Given the clinical relevance of tobramycin (Tob), an antibiotic, it was selected as the small model molecule. The bactericidal activity of both GaP-LL37 and GaP-Tob conjugates were assessed through both time-kill assays and colony-forming units (CFU) enumeration. In addition, human lung epithelial cell line A549 was selected as the model for biocompatibility studies.

Results: Three different types of GaP nanoparticles were screened as nanocarriers for LL37, all of which demonstrated loading efficiencies exceeding 90%. Morphological changes were observed in both GaP-LL37 and GaP-Tob conjugates, indicating successful conjugation. Fourier-transform infrared spectroscopy (FTIR) further confirmed the successful loading of LL37 and Tob onto the GaP nanocarriers. In terms of antibacterial efficacy, GaP-LL37 achieved a 2-log reduction in CFU compared to GaP NPs alone. Notably, GaP-Tob conjugates completely inhibited bacterial growth at a minimum concentration of 15 μg/mL, whereas GaP NPs alone required a concentration of 62 μg/mL to achieve the same effect.

Conclusion: Both macromolecules, LL37, and small molecule, tobramycin were successfully loaded onto GaP NPs. The GaP-LL37 and GaP-Tob conjugates exhibited enhanced antibacterial activities compared to GaP NPs alone.

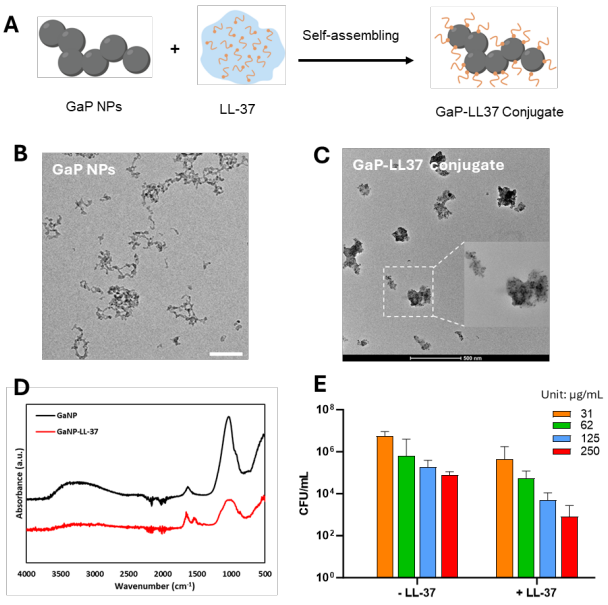
A
GaP NPs
+
LL-37
Self-assembling
GaP-LL37 Conjugate
B
GaP NPs
C
GaP-LL37 conjugate
D
GaNP
GaNP-LL-37
Absorbance (a.u.)
4000
3500
3000
2500
2000
1500
1000
500
Wavenumber (cm-1)
E
Unit: μg/mL
31
62
125
250
CFU/mL
10^8
10^6
10^4
10^2
10^0
- LL-37
+ LL-37

Figure 1.png

Targeted Nanoparticles for Non-invasive Diagnosis of Inflammatory Bowel Disease with Magnetic Resonance Imaging

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 166

anano maisuradze [1], ***Alexandra Teleki*** [1]

1. *Uppsala University*

Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, is a chronic inflammatory disorder of the intestines. Current diagnostic method-endoscopy are invasive, costly, and often require anesthesia in children(1). Magnetic Resonance Imaging (MRI) is a promising non-invasive alternative, but faces challenges in detecting mucosal changes and subtle inflammation. Orally administered superparamagnetic iron oxide nanoparticles (SPIONs) function as contrast agents for MRI of the gastrointestinal tract. Moreover, SPION surface functionalization allows targeting of specific biomarkers (2).

Our research aims to use SPIONs as targeted contrast agents for MRI to diagnose IBD. Our lab previously performed ex vivo and in vitro experiments utilizing antibody-conjugated SPIONs to target ICAM1 or CEACAM1, apical plasma membrane biomarkers for IBD(3). The SPIONs effectively targeted ICAM1 in inflammatory Caco2 cells(4). Ex vivo studies with mice with Dextran Sodium Sulfate-induced colitis showed that in modestly inflamed areas, SPIONs were trapped in mucus, unable to reach underlying cellular targets(3). Furthermore, antibody conjugation caused SPION aggregation, hindering transport through mucus.

Building on these results, SPIONs were functionalized with high-molecular-weight Polyethylene Glycol (PEG), which has been shown to improve nanoparticle penetration through mucus(5). Furthermore, an alternative targeting ligand, Arginylglycylaspartic acid (RGD) peptide, was conjugated with SPIONs. RGD peptide is a motif that binds to cell adhesion integrins that are overexpressed in endothelial tissue during inflammation. RGD peptide holds great promise in targeted drug delivery and imaging due to its ability selectively target integrin-overexpressing cells(5).

PEG-RGD conjugation increased the colloidal stability of SPIONs in biologically relevant media. Ongoing efforts aim to evaluate if PEG-RGD conjugation can ensure effective transport through artificial canine mucus(6). In vitro and in vivo studies will investigate the targeting capabilities of PEG-RGD-conjugated SPIONs(3).

In conclusion, SPIONs are promising MRI bioimaging agents and can improve diagnostic methods for IBD.

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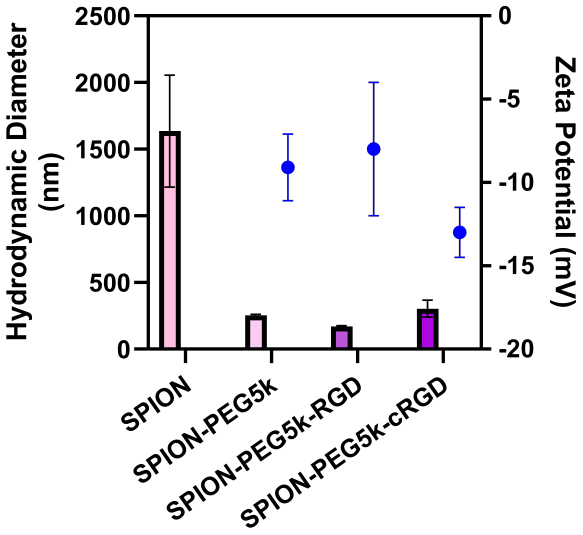


Size of Particles in Cell Culture Media (10% FBS)

Size of particles in ccm.png

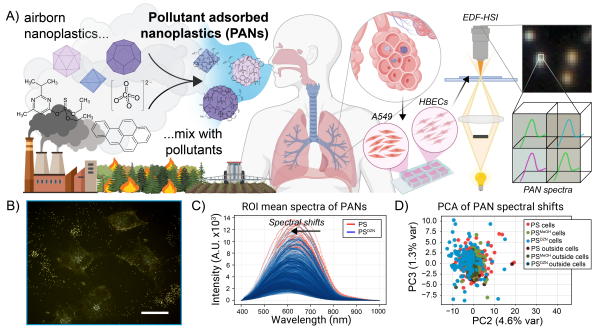
Physicochemical-dependent transportation of pollutant adsorbed nanoplastic (PANs) in lung cells

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 194

Elizabeth Hale [1], ***Eli Wooliever*** [1], ***Sascha Nicklisch*** [1], ***Randy Carney*** [1]

1. *University of California, Davis*

Only 9% of the estimated 8.3 billion tons of plastic on earth is recycled, leaving the rest to accumulate in the environment, where it ultimately degrades into micro- and nano-sized particles. Microplastics are established vectors for pollutants like pesticides and industrial chemicals, forming composite materials that pose great risks to human health, and sparking regulatory initiatives. Compared to microplastics, smaller **nanoplastics (<1 µm)** can travel over long distances in the atmosphere and possess altered health risks via lung inhalation. Moreover, their increased surface area-to-volume ratio enhances pollutant adsorption, forming **pollutant-adsorbed nanoplastics, or PANs**. Nanoplastics have been linked to cancer progression by inducing pro-inflammatory responses, endocrine disruption, and oxidative stress, yet the alteration of these cellular functions as a result of nanoplastic interplay with small molecule pollutants found in complex atmospheric particulate matter (i.e., formation of PANs) is poorly understood. The physicochemical interactions between pollutants and plastics drive PAN formation and their transportation and toxicity in the body, yet little is known regarding their formation kinetics, affinities, and cell trafficking mechanisms. This research applies enhanced darkfield hyperspectral imaging (EDF-HSI) as a label-free approach for single-particle tracking, resolving composition, desorption, and localization in cells to reveal how PANs exacerbate pollutant toxicity and carcinogenicity. EDF-HSI was used to chemically detect and spatially map spectral shifts in 220 nm polystyrene diazinon (PS^{DZN}) PANs compared to pristine PS controls, revealing significant adsorption heterogeneity amongst individual particles (**Fig. 1C**). Principle component analysis (PCA) revealed clustering of PS^{DZN} compared to pristine PS. We evaluated changes in cell uptake of PS^{DZN}PANs compared to controls of PS and PS with methanol solvent (PS^{MeOH}) in human lung adenocarcinoma (A549) cells. Quantification of particle counts within cells showed trends of increased uptake for PS^{DZN} compared to controls. Mean particle spectra were stratified by exposure condition and in/outside of cells for each exposure condition, revealing distinct spectral shifts for PS^{DZN}, indicating partial retention of DZN following uptake. These data establish the feasibility of EDF-HSI for non-destructive, label-free, single-particle spatial and chemical characterization of PAN formation kinetics and interactions in cells, and highlight the significance of pollutant adsorption on nanoplastic transportation in cells.



A) Schematic of premise of pollutant adsorbed nanoplastic (PAN) formation in the environment and trafficking to the lung post inhalation, and experimental design using enhanced darkfield hyperspectral imaging (EDF-HSI) to characterize PAN spectral shifts in *in vitro* cultures of human lung adenocarcinoma cells (A549s), and human bronchial epithelial cells (HBECs). Icons created with biorender.com. **B)** EDF image of altered intracellular trafficking of PS^{DZN} in A549 cells (scale bar = 10 µm). **C)** Mean spectra of PS (red) and PS^{DZN} (blue) particle regions of interest (ROIs). **D)** Principle component analysis (PCA) of particle spectra of (polystyrene-diazinon) PS^{DZN} PANs compared to PS and (PS-methanol) PS^{MeOH}.

Iconan2026 abstract fig.png

Cell-cell interaction via nanobody-receptor binding

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 204

Thu Ha Ngo [1], ***Alicja Przybyszewska-Podstawka*** [2], ***Shima Bourang*** [1], ***Adolfo Rivero-Müller*** [1]

1. *Department of Biochemistry and Molecular Biology, Medical University of Lublin,* ***2.*** *Department of Molecular Biology, Institute of Biochemistry, University of Warsaw*

Nanobodies are single domain antigen-binding antibody fragments (VHHs). With their small size (~15 kDa), high specificity, and ease of production, nanobodies show great promise for targeting molecules involved in cell signaling pathways, contributing to biomedical diagnostics and therapy.

Inspired by nanobodies capable of binding fluorescent proteins used for imaging and diagnostics, such as LaG nanobodies isolated from llamas, we investigated cell–cell interactions mediated by ligand–receptor binding using nanobody-based tools.

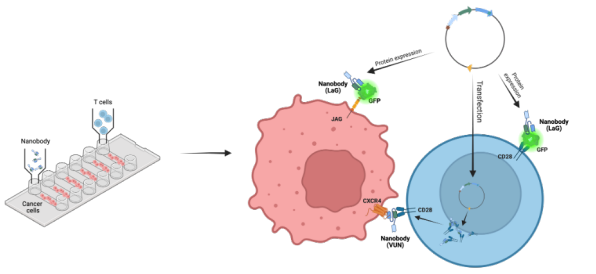
To induce the interactions between 2 cells, we fused nanobodies (LaG2 and LaG16) to the extracellular region of the transmembrane proteins JAG (ligand for Notch) and CD28, while presenting their antigen, GFP, on the membrane of the second cell, fused with CD28. Using these systems, we show that cell-cell contact can be promoted. We also show that nanobodies can bind GFP presenting-cells under flow in a microfluidic chip.

Then, we created a system where CXCR4-binding nanobodies (VUN400 and VUN410), fused to CD28, were used to direct the interactions between the nanobody-expressing cells and the CXCR4-expressing cells while flowing in a microfluidic device.

Since GPCRs, and CXCR4 in particular, are implicated in cell migration, immune cell trafficking, and the development of the central nervous and cardiovascular systems, they are major targets of current anticancer drugs, and therefore potential targets for immune- and cellular-therapies.

By generating cell-cell contacts between selected cells even under flowing conditions, we show that it is possible to study such interactions and determine the best targets, a potential approach to studying the interactions between e.g. immune cells and cancer cells.

Keywords: cell-cell interaction, CXCR4, GPCRs, nanobody, T cells, immunotherapy.



Schematic illustration of cell–cell interactions mediated by nanobody–receptor binding in a microfluidic chip. Nanobodies LaG2 and LaG16 were produced in bacteria on a large scale, while VUN400 and VUN410 are fused with the CD28 transmembrane domain and expressed on the cell membrane via transfection. Cell interactions occur within the microfluidic chip, where cancer cells are seeded, and nanobodies or T cells flow through the channel.

Schematic illustration of cell-cell interactions.png

Engineering bacteria-propelled giant vesicles as controllable micro-transport systems

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 227

Jyoti Gurung [1], ***Yuval Elani*** [1]

1. *Department of Chemical Engineering, Imperial College London, UK*

Biohybrid systems combining living microorganisms with synthetic vesicles offer powerful new strategies for targeted delivery and active matter design. Giant Unilamellar Vesicles (GUVs) were selected as the synthetic chassis due to their cell-like size, tuneable membrane mechanics, and large therapeutic loading capacity, features that make them more suitable than SUVs or LUVs for biomedical applications. Functional GUVs containing DOPC, DPPC, cholesterol, and either biotin-PE or Ni-NTA-DGS enabled specific attachment of motile Escherichia coli. Binding was achieved through streptavidin–biotin coupling to outer-membrane Antigen-43 or His-tag coordination with Ni^{2+} groups. Phase-separated GUVs further localized adhesion sites to liquid-ordered domains, creating asymmetric attachment geometries.

We demonstrate that attached bacteria remain motile and effectively propel the GUVs, forming an active biohybrid. Importantly, phase-separated GUVs enhance directional propulsion by biasing force generation toward clustered domains. To introduce external control, we employed Proteorhodopsin-based photoactivated motility, enabling reversible, light-controlled propulsion of the biohybrids.

These results highlight how membrane phase behaviour and optogenetic control synergize to regulate bacterial force transmission and navigation. Overall, GUV–bacteria assemblies represent a versatile platform for programmable microscale transport, targeted therapeutics, and bottom-up construction of synthetic living systems.

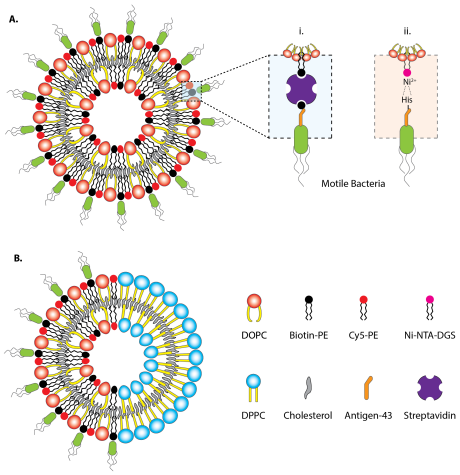


Figure1 jyoti.png

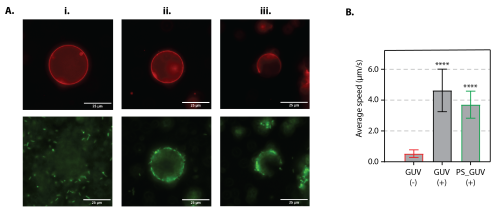


Figure2 jyoti.png

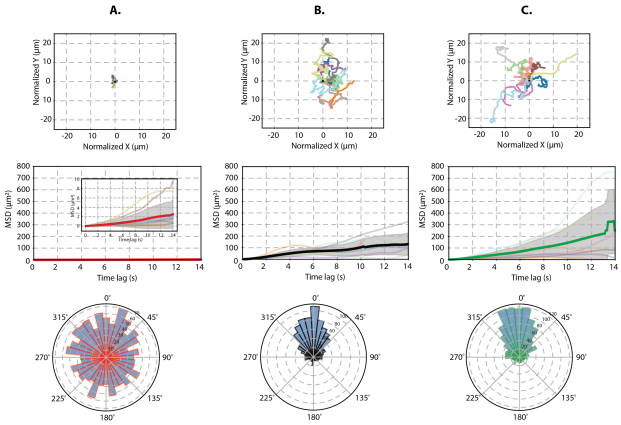


Figure3 jyoti.png

Medical devices loaded with biological active compounds as potential regenerative patches in wound healing

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 235

Anca Roseanu [1], ***Madalina Icriverzi*** [1], ***Paula Ecaterina Florian*** [1], ***Oana Gherasim*** [2], ***Valentina Gurmazescu*** [2], ***Gabriel Socol*** [2], ***Fabiola Ionita*** [3], ***Cristin Coman*** [3]

1. *Institute of Biochemistry of the Romanian Academy,* ***2.*** *National Institute for Lasers, Plasma and Radiation Physics,* ***3.*** *'Cantacuzino' National Medico-Military Institute for Research and Development*

Introduction: The skin wound healing is one of the most complex physiological processes in the human body and any aberration in its development may affect the normal physical function of skin. Topical application using patches with the capability of promoting dermis regeneration is attractive for full-thickness wound, due to reducing adverse effects. Here we propose a new formulation based on chitosan and polyethylene glycol (PEG), loaded with anti-inflammatory, antioxidant and antimicrobial compounds and its *in vitro* and *in vivo* wound healing potential evaluated.

Methods: Ibuprofen (IBUP)-loaded composite coatings were obtained by drop-cast method and the release profile of drug and degradation rate of polymer matrix using UV-Vis spectrophotometry, mass loss variation and scanning electron microscopy (SEM) were measured. Cellular viability and proliferation of human macrophages were assessed by colorimetric non-radioactive assay (MTS). Cytokines secretion by macrophages stimulated with bacterial endotoxins was measurement by enzyme-linked immunosorbent assay (ELISA). In vivo investigations were performed on rats for 14 days measuring the average wound area every 48h and histological and immunohistochemically analysis of wounds/ scars samples post treatment evaluated.

Results: The uniform PEG:IBUP coatings resulted in slowly and progressive release of the drug and emphasized a pronounced IBUP release starting from day 10 of dynamic evaluation. No cytotoxic effect was found in the presence of the new patches, the viability and proliferation of human macrophages being not affected. A reduced pro-inflammatory TNF-a cytokine release by macrophages was obtained. The *in vivo* studies showed that on day 14, healing process was similar for the animal groups treated with either new or standard Hartmann patches, respectively. Clinical analysis of blood samples and histopathological examination of skin samples revealed a reduced number of inflammatory cells and no bacterial colonization. Topical application of the proposed patches increased collagen synthesis, stimulated re-epithelialisation and accelerated wound healing process.

Conclusions: Collectively, our study provides evidence that the new patches through its physical-chemical and biological characteristics could be a valuable option for topical treatment of skin injures.

Acknowledgement: This research received funding from Romanian National Authority for Scientific Research under the projects TERAMED, and partial support of the Romanian Academy

Characterization of extracellular vesicles released by circulating tumor cells from pancreatic cancer patients

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 241

Rita Palieri [1], ***Maria De Luca*** [2], ***Francesco Balestra*** [2], ***Giorgia Panzetta*** [2], ***Federica Rizzi*** [3], ***Maria Lucia Curri*** [4], ***Luigi Andrea Giuseppe Laghi*** [5], ***Gianluigi Giannelli*** [6], ***Nicoletta Depalo*** [3], ***Maria Principia Scavo*** [2]

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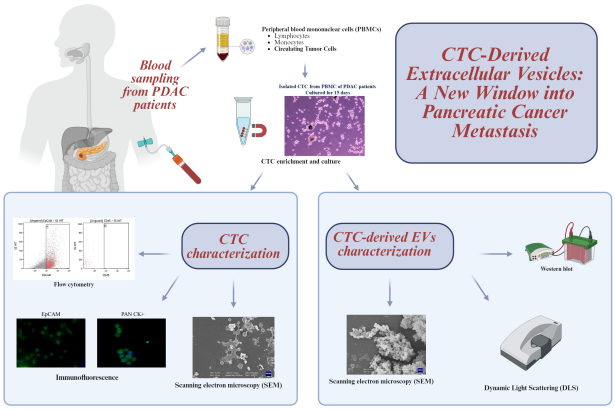
Background: Pancreatic ductal adenocarcinoma (PDAC) remains one of the most aggressive tumour, with limited options for early detection and monitoring. Circulating tumor cells (CTCs) and their secreted extracellular vesicles (EVs) represent promising sources of minimally invasive biomarkers. However, the molecular and functional features of EVs specifically derived from CTCs (CTC-EVs) in PDAC are still poorly understood.
Aim: This study aimed to isolate and characterize CTCs and their EVs obtained from the peripheral blood of pancreatic cancer patients, and explore their potential as disease-specific biomarkers.
Methods: CTCs were isolated using an EpCAM-based immunomagnetic beads from blood samples of PDAC patients. After short-term culture, CTCs underwent citofluorimetry and immunofluorescence. EVs released into the conditioned medium were collected and characterized by Dynamic Light Scattering analysis (DLS), Scanning electron microscopy (SEM), and Western blot for canonical EV markers and tumor-related proteins. Comparative analyses were performed with EVs derived from tumor and non-tumor pancreatic cell lines (MIA-PaCa-2, PANC-1, HPDE).
Results: Flow cytometry confirmed tumor origin of cells (EpCAM+). They displayed a hybrid phenotype, co-expressing epithelial markers (EpCAM, CK18, CK19) and epithelial-to-mesenchymal transition drivers Vimentin and TWIST, indicating marked plasticity and metastatic potential. Preliminary data indicate that CTCs from PDAC patients release a heterogeneous population of EVs with an average size of 100–150 nm. Scanning electron microscopy revealed CTC surface architectures distinct from pancreatic cancer lines (MIA-PaCa-2, PANC-1), suggesting adaptations for haematogenous survival, while EVs exhibited intact, well-defined morphology. CTC-EVs express both general EV markers and tumor-associated proteins.
Conclusion: Our findings suggest that extracellular vesicles released by circulating tumor cells carry molecular and phenotypic signatures reflective of the metastatic behavior of pancreatic cancer. Further validation in larger cohorts could establish CTC-EVs as a novel liquid biopsy tool for disease monitoring and therapeutic stratification in PDAC.



Ctc s evs in pdac.jpeg

Optimizing drug delivery system for small peptide CAQK

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 261

Hanna Lavén [1], ***Qinglin Yang*** [2], ***Alexandra Teleki*** [3], ***Michael J Sailor*** [4]

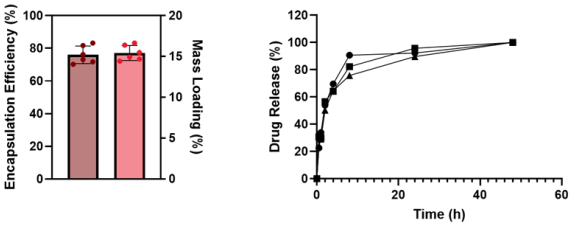
1. *1. Department of Pharmacy, Science for Life Laboratory, Uppsala University, Sweden 2. Advanced Drug Delivery, AstraZeneca R&D, Gothenburg, Sweden,* ***2.*** *Materials Science and Engineering Program, University of California San,* ***3.*** *Uppsala University,* ***4.*** *Department of Chemistry and biochemistry, University of California San Diego*

Introduction: The CAQK peptide has demonstrated an ability to bind specifically to chondroitin sulfate proteoglycans, molecules that are upregulated following brain or spinal cord injury. Beyond their targeting properties, recent research suggests that CAQK may also have therapeutic benefits for recovery after neural trauma[1]. However, effective delivery of therapeutic peptides to the brain remains challenging due to rapid drug clearance and the presence of physiological barriers. To overcome these challenges, nanoparticle delivery systems offer a promising strategy to transport CAQK to target sites within the brain[2]. In this work we aim to engineer a biocompatible, silicon-based porous carrier system for the sustained release of CAQK.

Methods: Porous silicon nanoparticles were fabricated by electrochemical etching of silicon wafers in an HF-based electrolyte, producing porous layers with different porosity through a perforated etch. The etched layers were lifted off and fragmented by sonication into nanoparticles. By changing the etching conditions, different porosity and particle sizes can be achieved. Porosity was estimated using the spectroscopic liquid infiltration method (SLIM), particle size was measured by dynamic light scattering (DLS) and confirmed by transmission electron microscopy (TEM), while pore size was assessed by cryogenic nitrogen adsorption/desorption isotherms and TEM.

Results: We optimized electrochemical etching conditions to provide porous silicon nanoparticles with diameters of 120 nm, porosity of 45% and a pore size of 8nm. CAQK was loaded into the porous silicon by hydrolytic trapping from an aqueous buffer solution. A mass loading of 15 % was achieved, with an encapsulation efficiency of 76 %. CAQK release into a phosphate buffered saline (PBS) solution maintained at 37 °C was studied; complete release after approximately 24 h was observed.

Next steps will include comparison of drug loading and release from porous silicon nanoparticles prepared via a thermal oxidation route.



Drugrelease caqk.png

Advancing Antimicrobial Nanoparticle Design: Antibiotic-Conjugated Hollow Gold Nanoparticles as Next-Generation Nanotherapeutics

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 282

Jack Homer [1], ***M. Alejandra Diaz de Rienzo*** [1], ***Chloe James*** [1], ***Zeljka Krpetic*** [1]

1. *School of Science Engineering and Environment, University of Salford, United Kingdom*

The continued rise of antimicrobial resistance has rendered many conventional antibiotics ineffective against key pathogenic bacteria, posing a major global health threat. Innovative strategies to combat bacterial infections are therefore urgently required. Nanoparticles offer a promising avenue due to their unique physicochemical properties that enable both therapeutic and diagnostic applications.

In this study, we investigated the antimicrobial potential of hollow gold nanoparticles (HAuNPs), focusing on how particle shape influences antimicrobial efficacy. A nanoparticle library was generated through systematic synthesis approaches, pairing different core materials with tailored surface chemistries to assess their combined effects on bacterial inhibition. The functionalised nanoparticles were evaluated against Staphylococcus aureus (ATCC 6538) and Pseudomonas aeruginosa (ATCC 27853) using a modified in-house serial broth dilution assay designed for nanomaterial testing. Our findings show that antibiotic-conjugated HAuNPs exhibited significantly enhanced antimicrobial activity compared to other nanoplatforms, namely solid gold and silver nanoparticles within the library and to the free antibiotic. These results highlight the critical role of nanoparticle shape as a design parameter in the development of next-generation antimicrobial nanoplatforms.

Advancing Cancer Nanotherapeutics with Functional Hollow Gold Nanoparticles for Efficient Drug Delivery

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 294

Yara Atto [1], ***Zeljka Krpetic*** [2], ***Alberto Martinez Serra*** [3], ***Marco Monopoli*** [4], ***Marija Krstic Demonacos*** [2]

1. *The Universty of Salford,* ***2.*** *Biomedical Research and Innovation Centre, School of Science Engineering and Environment, University of Salford, Manchester M5 4WT,* ***3.*** *Department of Chemistry, University of Medicine and Health Sciences, Royal College of Surgeons in Ireland, Dublin,* ***4.*** *Department of Chemistry, University of Medicine and Health Sciences, Royal College of Surgeons in Ireland, Dublin 2, Ireland*

ABSTRACT

Hollow gold nanoparticles (H-GNPs) represent an emerging class of nanocarriers with the potential to transform cancer nanotherapeutics. While gold nanoparticles are currently explored for drug delivery, the influence of nanoparticle morphology on bio-nano interactions within biological environments remains insufficiently understood. H-GNPs offer some advantages over other particles, including reduced cytotoxicity and tuneable structures that enable new strategies for drug encapsulation, conjugation and release.

In this work, we develop and optimise functionalisation strategies for engineered H-GNPs to carry established anticancer agents and compare their performance against conventional solid gold nanoparticles. A robust suite of complementary analytical approaches (UV-vis spectroscopy, Differential Centrifugal Sedimentation (DCS), Nanoparticle Tracking Analysis (NTA), High Performance Liquid Chromatography (HPLC), Dynamic Light Scattering (DLS), SDS-PAGE and Transmission Electron Microscopy (TEM)) was used to characterise particle morphology, surface chemistry, physico chemical stability in relevant media, and biomolecular corona formation, enabling a holistic evaluation of their bio-nano interface as well as their anticancer efficacy. Comparative *in vitro* studies using FACS and MTT assays across multiple cancer cell lines further assess therapeutic response and cellular uptake behaviour.

Our findings indicate that H-GNPs enhance anticancer activity at matched therapeutic dosages while showing improved selectivity relative to both free drug and solid GNP controls towards breast cancer cell lines, particularly a highly aggressive triple-negative breast cancer cell line MDA-MB-231. Distinct biomolecular corona fingerprints were observed for these particles, and correlation to their *in vitro* efficacy is being explored.

Overall, our functional H-GNP platform offers realistic opportunities for targeted delivery of the established cancer therapeutics into breast cancer cells, improved efficacy, and future application as multimodal theranostic systems.

Preliminary development of a hydrogel composition containing nanocarriers loaded with active substances for the treatment of skin diseases

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 274

Agnieszka Sobczak [1], ***Maria Urbańska*** [2], ***Jolanta Długaszewska*** [3], ***Anna Jelińska*** [1], ***Izabela Muszalska-Kolos*** [1], ***Ludwika Piwowarczyk*** [1]

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Inflammatory skin diseases, chronic and relapsing, like atopic dermatitis, psoriasis, acne, and eczema, represent a public health challenge and affect a substantial proportion of the global population. Despite the availability of numerous pharmaceutical products, a need remains for more effective and safer therapeutic approaches. One promising strategy in managing inflammatory dermatoses is the use of nanotechnology, which enables improved bioavailability and controlled delivery of active compounds.

The aim of the present work was to develop a new, effective dosage form – a hydrogel containing nanoformulation with plant-origin active substances. The first stage involved the qualitative and quantitative selection of hydrogel base ingredients and preservatives based on a preservative efficacy test, as per pharmacopeial requirements (Eur. Ph. 11th Edition). The developed base was characterized by analyzing density, viscosity, and pH. A plot of viscosity versus shear rate in a plate–plate measurement system (25 °C) exhibited characteristics typical of pseudoplastic non-Newtonian fluids. The apparent viscosity at a shear rate of 20 s^{-1} averaged 6255 mPa·s. The density determined at 25 °C was 1.0096 g/mL, and the pH of the base stored for two months at room temperature and in the refrigerator remained stable (4.67 – 4.93).

In the next step, developed nanoformulation with APIs, specifically ethosomes, was introduced into the hydrogel base. The resulting formulation exhibited an appropriate homogeneous consistency, enabling topical application. Analyses using cryo-TEM microscopy and nanoparticle tracking analysis (NTA) confirmed the presence of nanoparticles within the hydrogel structure and the absence of their destruction during the formulation process. In a two-month storage period at room temperature and in the refrigerator, no visual changes were observed, and the gels' pH remained within the range 4.99-5.22.

Funding: *Research aimed at developing a new, innovative pharmaceutical form for the topical treatment of psoriasis vulgaris" is being implemented as part of the National Recovery and Resilience Plan, as part of Investment D3.1.1 Comprehensive development of research in medical sciences and health sciences, reference number: 2024/ABM/03/KPO/KPOD.07.07-IW.07-0043/24-00.*

Development and Characterization of Transferosome-Based Formulations Containing 20-Hydroxyecdysone (HE) for Potential Dermatological Applications

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 268

Pawel Bakun [1]***, Szymon Tomczak*** [2]***, Dariusz T. Młynarczyk*** [1]***, Ludwika Piwowarczyk*** [2]

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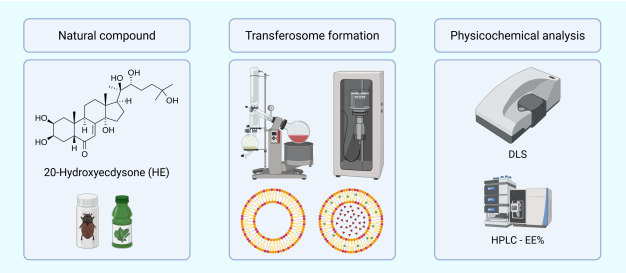
Natural compounds such as 20-Hydroxyecdysone (HE) are well recognized for their anti-inflammatory and regenerative properties, making them attractive candidates for topical treatment of skin disorders, including psoriasis. However, their poor skin permeability and limited stability present challenges for effective application. In this study, we developed and optimized transferosome-based formulations to enhance the dermal delivery of HE.

Transferosomes were prepared using a thin-film hydration method followed by probe sonication, employing phospholipids and edge activators tailored to specific properties of HE. Physicochemical characterization included measurements of particle size, polydispersity index (PDI), and zeta potential. Encapsulation efficiency (EE%) was determined using chromatographic techniques. Stability studies were conducted over a one-month period under controlled conditions, monitoring changes in size, PDI, and zeta potential.

This work demonstrates the feasibility of using transferosomes as carriers for natural bioactive compounds in dermatological applications. The optimized formulations offer a promising strategy for enhancing skin delivery and therapeutic efficacy of HE, paving the way for novel treatments of inflammatory skin diseases.

The authors would like to thank the Polish Medical Research Agency for funding the project under Grant No. 2024/ABM/03/KPO/KPOD.07.07-IW.07-0043/24-00, titled "*Research aimed at developing a new, innovative pharmaceutical form for the topical treatment of psoriasis vulgaris*".



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Isoniazid-loaded multicore magnetic nanoparticles as a facile intervention for combating mycobacterial infection.

Friday, 16th January - 13:30: Poster Session (Posters & Coffee Breaks) - Poster - Abstract ID: 77

Lipsa Leena Panigrahi [1], Ashirbad Sarangi [2], Bhabani Shankar Das [3], Shashank Shekhar [4], Debapriya Bhattacharya [5], Manoranjan Arakha [3]

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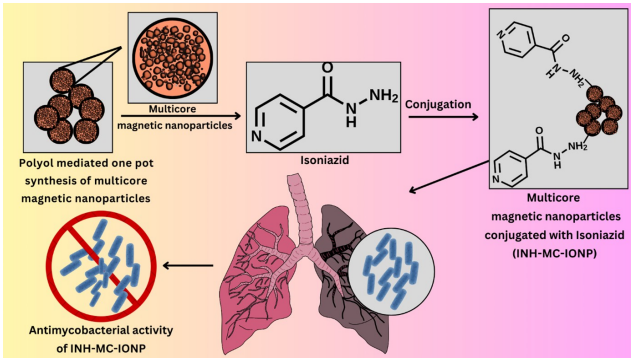
A hybrid first-line tuberculosis antibiotic conjugated programable magnetic nanoplatform for application in precision therapeutics for treating tuberculosis (TB) is described. Here the citrate anions grafted multicore magnetic nanoparticles (MC-IONP) steer the precise delivery of isoniazid (INH). This approach promotes specificity and synergistically improves the accumulation of isoniazid upon the bacterial membrane interface thus avoiding the need for higher doses for the treatment. Despite the wide use of isoniazid, there has been no optimal dose established for the treatment of TB which has led to inadequacy in treatment outcomes. Also, the poor drug absorption and lack of proper knowledge of the pharmacokinetics of INH had made the rise of INH-resistant mycobacteria inevitable. The conjugation of INH upon MC-IONP is facilitated by electrostatic interaction. The successful conjugation was analysed using FTIR and zeta/DLS. The nanoconjugates exhibited MIC at 1.5 mg/mL and MBC at 3.12 mg/mL. The nanoconjugates were stable up to 72 hrs and showed significant inhibition of replicating bacteria in growth kinetics assay. an increase in ROS formation is noted in cells treated with INH-MC-IONP nanoconjugates. In the biofilm model, the mycobacterial biofilm is significantly inhibited (96%) at a concentration of 12.25 mg/mL. The nanoconjugate is also effective against persistent mycobacteria. Given these prevailing scenarios the data obtained suggest that this hybrid nanoplatform acts as a promising tool for application in enhancing the effects of INH with lower doses possible.

New concept

Notably, our approach consists of (i) the single core size was about 8-10 nm which cooperated magnetically to form multicore nanoparticles of size about 30-50 nm. (ii) the cooperative magnetic behavior within highly crystalline multicore magnetic particles subsequently improves therapeutics and diagnostics effectiveness over existing nanostructures when conjugated with a generalized drug. (iii) The mycobacterial targeting efficacy of our strategy impacts the replicating, biofilm, persistent, and dormancy phases of mycobacterium species. Thus, our finding opens new insights for the use of novel engineered nanoplatforms for the treatment of TB.



Graphical abstract.jpg

Impact of Short PAS Domain Functionalization on the Structural Stability of H-Ferritin Nanocages

Friday, 16th January - 14:30: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 264

Francesca Gorgoglione [1], ***Ilaria Tagliolini*** [1], ***Marta Sevieri*** [2], ***Beatrice Bignami*** [1], ***Valeria Giacobbo*** [2], ***Claudia Pigliacelli*** [3], ***Francesca Baldelli Bombelli*** [3], ***Fabio Corsi*** [4], ***Renata Tisi*** [5], ***Serena Mazzucchelli*** [6]

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Nanomedicine is a rapidly advancing field, particularly in oncology, where it enables targeted delivery of anti-cancer agents to improve efficacy and minimize systemic toxicity. Among emerging nanocarriers, recombinant nanocages composed of the H-chains of human ferritin (HFn) have shown great promise due to their intrinsic tumor tropism and excellent biocompatibility. Despite these advantages, their clinical translation is limited by their short circulation half-life and rapid clearance. Functionalization with unstructured PAS polypeptides, rich in Proline, Alanine and Serine of 40 and 75 amino acids, designed to be cleaved by tumor-associated metalloproteinases (MMPs), has previously been shown to extend systemic circulation while preserving tumor-targeting. In this study, we investigated the impact of shorter PAS domains on HFn stability by engineering a mutant containing PAS domains of 20 amino acids (PAS20-HFn) and comparing it with the established PAS40-HFn mutant. Both variants were successfully produced in *E. coli* and purified using ion exchange chromatography (IEC). While PAS40-HFn maintained its ability to form stable nanocages, PAS20-HFn failed to assemble into quaternary structures after purification, although cage-like assemblies were observed in crude extracts. This suggests that electrostatic interactions during IEC may destabilize the PAS20-HFn nanocage. To elucidate this behavior, molecular dynamics simulations were conducted at the dimer, tetramer, and octamer levels for both mutants. PAS20-HFn exhibited increased flexibility in the C-terminal region encompassing the D–E helical interface, which is essential for dimer–dimer interactions and higher-order assembly. During octamer formation, interactions between PAS20 domains and adjacent C-terminal regions disrupted the alignment of E-helices, resulting in nanocage instability. In contrast, PAS40-HFn displayed reduced mobility and greater structural stability, consistent with its successful nanocage formation under the same experimental conditions. These findings demonstrate that PAS length plays a critical role in determining the structural integrity of HFn nanocages, establishing it as a key parameter in the design of PASylated HFn-based nanocarriers. Optimizing PAS length is therefore essential to achieve a balance between extended circulation time and structural stability, ensuring effective performance in theranostic applications.

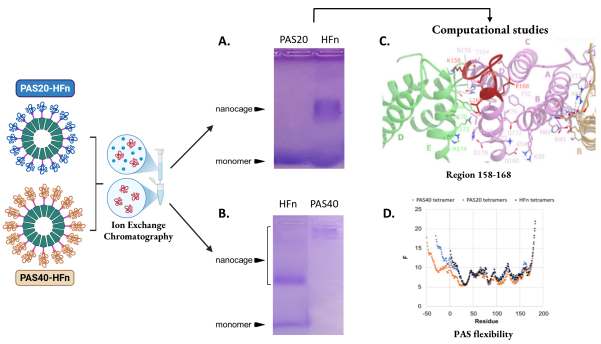

Figure 1. Production of PAS20-HFn and PAS40-HFn mutants and computational studies. **A)** Agarose gel characterization of PAS20-HFn achieved after IEC revealed the absence of nanocages compared to the correctly folded HFn due to instability of the quaternary structure. **B)** Agarose gel characterization of PAS40-HFn following IEC confirmed the presence of nanocages. **C)** Molecular dynamics representation of the 158–168 region (in red) located near the C-terminus of HFn, involved in tetramer stabilization and nanocage assembly. **D)** Fluctuation plot obtained from molecular dynamics simulations. The analysis revealed higher flexibility in the PAS20 domain compared to PAS40 (left side of the plot, residues < 0). The enhanced flexibility of the PAS20 domain induces the separation of dimer–dimer interface regions, thereby weakening the stabilizing interactions essential for quaternary structure integrity.

Figure 1. production of pas20-hfn and pas40-hfn mutants and computational studies..png

STORM as a tool to track cargo release from polymeric nanocarriers at the single-particle level

Friday, 16th January - 14:46: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 192

Anna Solé Porta [1], ***Sílvia Pujals*** [2], ***Pietro Delcanale*** [3], ***Anna Roig*** [1]

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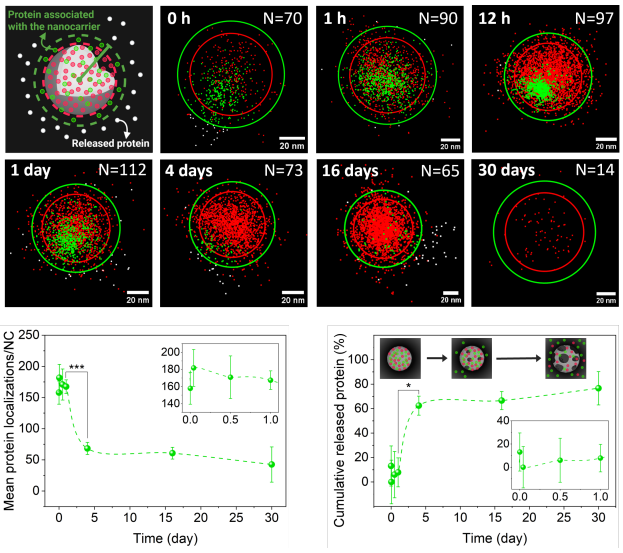
Recent advances in super-resolution microscopy have enabled unprecedented visualization of cellular structures, tracking of nanomaterials in biological environments, or the elucidation of specific nano-bio interactions. Yet, dynamic quantification of cargo release from individual nanocarriers remains unexplored. Here, we take advantage of the high spatial resolution of stochastic optical reconstruction microscopy (STORM) for real-time monitoring of protein release at the single-nanocarrier level. Poly(lactic-co-glycolic acid) (PLGA) nanocapsules with Cyanine5 loaded with bovine serum albumin tagged with Alexa Fluor 488 are characterized using STORM alongside cryo-TEM, STEM-EDX, SEM, and nanoparticle tracking analysis. STORM allowed us the simultaneous observation of several nanocarrier properties over time, including size, morphology, and cargo localization. Our results demonstrate a time-dependent increase in nanocapsule diameter and a decrease in nanocarrier concentration. The MATLAB-based quantitative analysis of individual nanocarriers reveals single-particle protein release profiles, exhibiting an initial burst followed by sustained release, reaching 80% cumulative release after 30 days. This study represents the first application of STORM to spatially and temporally resolve protein release from nanocarriers, offering single-molecule sensitivity and nanometric resolution, and capturing heterogeneity that ensemble-averaged techniques overlook. Our approach complements other pharmacokinetic analyses and establishes a foundation for optimizing therapeutic delivery systems at the single-particle level.



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Silica Nanoencapsulation: A Sustainable Breakthrough for DNA Preservation and Delivery

Friday, 16th January - 15:02: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 172

Mónica L. Fanarraga [1]

1. *Universidad de Cantabria-IDIVAL*

Current DNA storage depends on ultra-low temperature (ULT) freezers, leading to high operational costs, massive energy use, and significant environmental impact. We present a sustainable and transformative alternative: the encapsulation of nucleic acids within solid, water-soluble silica nanoparticles (**DNA@SiO$_2$**), a patented nanosystem (ES2934282A1) designed to replace conventional cold storage and enable new therapeutic applications.

This platform creates a protective, amber-like matrix that stabilizes DNA at ambient temperature, providing exceptional resistance to heat (90 °C), nucleases, reactive oxygen species, and acidic conditions. By removing the need for an energy-intensive cold chain, it drastically reduces CO_2 emissions, storage costs, and sample loss risk—offering a reliable solution for long-term preservation and transport of genetic material.

Beyond stabilization, **DNA@SiO$_2$** nanoparticles are engineered for controlled dissolution in physiological buffers, ensuring rapid and intact nucleic acid release. This dual functionality transforms the system into a versatile, non-viral vector for gene transfer, vaccination, and targeted delivery of therapeutic oligonucleotides (ASOs) or oligonucleotide prodrugs. We will present validation data demonstrating successful delivery of plasmids, linear DNA fragments, and small prodrug oligos, supported by preclinical studies.

Conclusion: Silica nanoencapsulation provides a robust, cost-efficient, and environmentally sustainable platform that simultaneously revolutionizes DNA storage and biobanking and expands the toolbox for nucleic acid delivery in biotechnology and medicine.

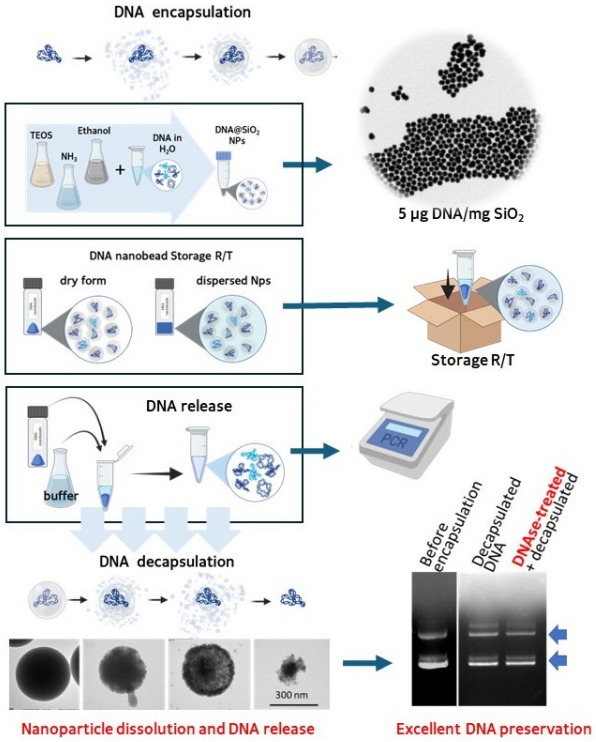

DNA encapsulation
TEOS
Ethanol
NH3
DNA in H2O
DNA@SiO2 NPs
5 µg DNA/mg SiO2
DNA nanobead Storage R/T
dry form
dispersed Nps
Storage R/T
DNA release
buffer
PCR
DNA decapsulation
Before encapsulation
Decapsulated DNA
DNAse-treated + decapsulated
300 nm
Nanoparticle dissolution and DNA release
Excellent DNA preservation

Figura3.jpg

Biocompatible urease-powered nanobots for personalized bladder cancer therapy

Friday, 16th January - 15:18: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 165

Inés Macías Tarrío [1], ***Nuria Sabando*** [2], ***Valerio Di Carlo*** [1], ***Kristin Fichna*** [1], ***Carles Prado*** [3], ***Oriol Jutglar*** [1], ***Esther Julián*** [2], ***Samuel Sánchez*** [1]

1. *Institute for Bioengineering of Catalonia (IBEC),* ***2.*** *Universitat Autonoma de Barcelona,* ***3.*** *IBEC*

The effective delivery of anticancer drugs remains a critical clinical challenge due to factors such as degradation in biological environments, limited tumor penetration, and poor targeting of cancer cells. Specifically, in non-muscle invasive bladder cancer (NMIBC), the efficacy of intravesical therapies is further compromised by drug sedimentation and rapid elimination from the bladder via urination, leading to high recurrence rates and poor long-term survival in patients.

Urease-powered nanobots (NBs) — self-propelled nanoparticles that harness urea for autonomous motion — have emerged as a promising strategy to overcome these limitations. By utilizing the urea present in the bladder, these NBs can actively navigate toward tumor sites, enhance nanoparticles local retention, and improve drug delivery compared to standard therapies and passive particles. However, current NB designs often rely on inorganic materials and are loaded with conventional chemotherapies, underscoring the need for more biocompatible and personalized formulations.

Here, we introduce a novel formulation of urease-powered nanobots composed of poly(lactic-co-glycolic acid) (PLGA) loaded with Erdafitinib, a selective inhibitor of fibroblast growth factor receptor 3 (FGFR3), commonly altered in NMIBC. NBs were synthetized, loaded with erdafitinib and functionalized with urease to enable self-propulsion in urea-rich environments. NB motion, cellular uptake, therapeutic efficacy and mechanisms of action were evaluated using NMIBC mice cells (MB49 cells). Finally, we performed in vivo experiments in which NBs were administered intravesical and survival and tumor volume were evaluated over 2 months.

Our results demonstrate that the nanobots exhibit enhanced propulsion in the presence of urea and significantly increased cellular uptake compared to passive particles. In addition, drug delivery via NBs resulted in a 9-fold reduction in the IC_{50} of Erdafitinib. In vitro studies revealed that the NBs induced S-phase cell cycle arrest and rapid apoptosis, consistent with the known mechanisms of Erdafitinib. Finally, in a murine model of bladder cancer, intravesical administration of the NBs led to effective tumor suppression, prevention of recurrence, and an 86% survival rate over two months, with complete tumor eradication observed in treated animals.

Collectively, these findings demonstrate the potential of our biocompatible, urease-powered nanobots as an effective and personalized intravesical therapy platform for NMIBC.

Evaluation of the antineoplastic efficacy of H-Ferritin–linked monoclonal antibodies in 3D tumor culture systems

Friday, 16th January - 15:34: Prevention and Treatment of Diseases (Auditorium) - Oral - Abstract ID: 141

Linda Barbieri [1]***, miriam colombo*** [1]***, Davide Prosperi*** [2]

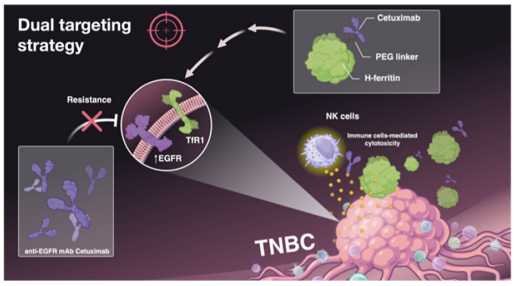
1. *University of Milano-Bicocca,* ***2.*** *University of Milan Bicocca*

Cetuximab (CTX) is an anti-EGFR monoclonal antibody with proven efficacy against EGFR-positive cancers. However, mutations in the Ras-ERK and PI3K-AKT pathways often confer primary or acquired resistance, limiting CTX effectiveness in tumors such as glioblastoma and triple negative breast cancer (TNBC), which lack alternative molecular targets. Here, we present a dual-targeting strategy that employs H-Ferritin (HFn) nanoconjugates to repurpose CTX for CTX-resistant cancers. This approach combines the TfR1-targeting capacity of HFn – TfR1 being overexpressed in most solid tumors – with the EGFR-binding and immune-mediated cytotoxic activity of CTX.

The HFn-CTX nanoconjugate markedly enhanced CTX antitumor efficacy in refractory TNBC spheroids, inducing a stronger antibody-dependent cellular cytotoxicity (ADCC) response than CTX alone. In contrast, no such effect was observed in glioblastoma spheroids, suggesting that cell-type specific factors modulate nanoconjugate activity. We identified the cell-surface expression of EGFR and TfR1 as key determinants of this difference. In U87-MG glioblastoma cells, high TfR1 levels drive constitutive clathrin-mediated endocytosis (CME) and recycling, while low membrane EGFR reduces ligand-induced uptake. Conversely, in MDA-MB-231 TNBC cells, slower caveolin-mediated internalization of CTX-bound, ligand-free EGFR allows the HFn-CTX nanoconjugate to remain longer on the plasma membrane, thereby enhancing ADCC. These findings explain the distinct immune responses observed between cell types.

Beyond mechanistic insights, the HFn-CTX nanoconjugate exhibited favorable physicochemical properties, including a hydrodynamic diameter below 30 nm, enabling efficient tumor penetration and superior biodistribution in vivo. Its enhanced accumulation in TNBC tumors likely results from the combined effects of small size and dual receptor targeting.

Overall, this study demonstrates that HFn-based conjugation can overcome CTX resistance in TNBC by enhancing immune-mediated cytotoxicity and tumor selectivity. More broadly, it highlights the potential of nanotechnology to improve monoclonal antibody therapies by optimizing pharmacokinetics, tumor penetration, and specificity. The modular HFn platform also allows functionalization with other therapeutic agents, extending its applicability beyond TNBC. Thus, HFn–CTX emerges as a promising candidate for next-generation nanomedicine approaches to enhance the clinical success of CTX-based therapies in resistant cancers.



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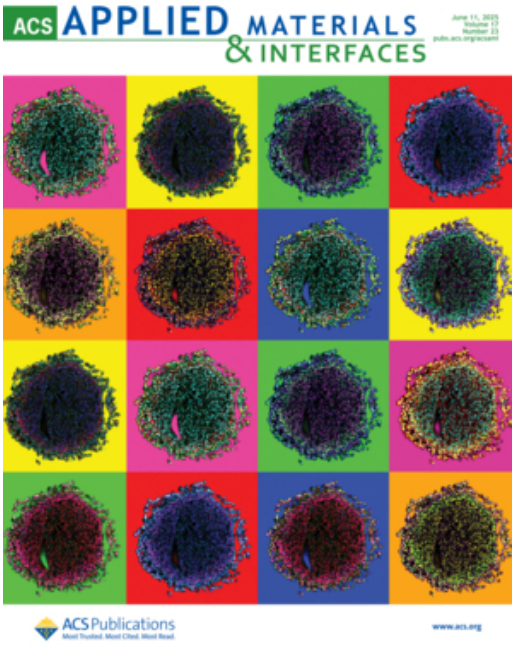

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Printable Functional Skin Analogs with Spatiotemporal Healing Orchestration

Friday, 16th January - 15:50: Prevention and Treatment of Diseases (Auditorium) - Invited Speaker - Abstract ID: 320

Nan Xu [1]

1. *Southern University of Science and Technology*

Full-thickness skin injuries remain a major clinical challenge due to the lack of functional grafts and the limitations of current biomaterials. To address this, we developed a digital light processing (DLP)-based bioprinting strategy to fabricate tri-layered skin constructs that replicate the epidermis, dermis, and hypodermis, each possessing distinct biochemical and mechanical properties.

Our approach integrates multi-material bioink design, printing parameter optimization, and spatiotemporal growth factor delivery to achieve both structural fidelity and biological functionality. Using a multi-step DLP bioprinting process, the layers were sequentially fabricated with photo-curable poly (β-amino ester) (PBAE) resins synthesized via Michael addition, enabling tunable degradation and mechanical behavior. The epidermal analog enhanced hydration and keratinocyte proliferation, the dermal analog promoted fibroblast infiltration and collagen deposition, while the hypodermal analog reproduced the elasticity and cushioning of adipose tissue.

Moreover, our delivery strategy enables layer-specific and cell-targeted cytokine release at the wound site, allowing precise regulation of macrophage subtype function and promoting the transition from M2a to M2c phenotypes during chronic wound healing.

The resulting tri-layered constructs exhibited well-defined mechanical gradients, layer-specific cellular organization, and accelerated wound healing, closely mimicking the natural architecture and regenerative dynamics of human skin. This system demonstrates the feasibility of fabricating complex, living, multi-material tissues with high precision and provides a versatile platform for spatially and temporally coordinated regeneration.

In summary, our work establishes a functional, biomimetic skin bioprinting system that overcomes the limitations of monolithic materials and uncontrolled healing. It represents a significant step toward clinically viable, patient-specific skin substitutes for advanced wound care and regenerative medicine applications.

E-cadherin–Functionalized Magnetic Nanoparticles for Controlled Guidance of Induced Pluripotent Stem Cell Differentiation

Friday, 16th January - 14:30: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 303

Christian Castro-Hinojosa [1], ***Susel Del Sol-Fernández*** [1], ***Pablo Martínez-Vicente*** [1], ***Nadia Roumans*** [2], ***Vanessa LaPointe*** [2], ***Raluca Fratila*** [1], ***María Moros*** [1]

1. *Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza, Zaragoza 50009, Spain,* ***2.*** *Cell Biology-Inspired Tissue Engineering, MERLN Institute for Technology-Inspired Regenerative Medicine, Maastricht, Maastricht, Limburg, Netherlands.*

The capacity to remotely and precisely control intracellular signaling pathways offers powerful opportunities for both fundamental biological research and therapeutic innovation. Among these pathways, Hippo and transforming growth factor-beta (TGF-ß) are key regulators of cell proliferation and differentiation. In stem cells, differentiation arise from a complex interplay between soluble factors, cell-cell interactions, and mechanical forces. Mechanical cues constitute crucial regulators of stem cell behavior, acting through diverse mechanotransduction mechanisms, including those associated with adhesion complexes. Within this framework, E-cadherin-mediated adhesions function as mechanosensitive hubs that integrate physical forces with intracellular pathways such as Hippo or TGF-ß. However, how mechanical stimulation of E-cadherin influences these pathways and affects stem cell fate remains incompletely understood.

Here, we introduce a novel strategy based on magnetic nanoparticles (MNPs) that enables remote, noninvasive, and tunable modulation of these pathways through targeted stimulation of E-cadherin. This approach establishes a tool at the interface of nanomaterials engineering and stem cell mechanobiology. We engineered octahedral MNPs ($Zn_{0.29}Mn_{0.18}Fe_{2.53}O_4$) bioconjugated with the extracellular domain of E-cadherin (MNPs@E/EC15) to specifically bind surface E-cadherin on iPSCs. Upon treatment, we observed pronounced nuclear translocation of YAP, the main effector of the Hippo pathway. Correspondingly, YAP-regulated genes *NODAL* and *WNT3* (both repressed by nuclear YAP) were significantly downregulated at 24- and 72-hours. Because *NODAL* is a key activator of the TGF-ß/SMAD2/3 axis, its downregulation correlated with decreased SMAD2/3 nuclear localization, confirming functional inhibition of this signaling branch. This modulation is consistent with early commitment of iPSCs toward a neuroectodermal lineage.

To further validate this effect, we applied the dual-SMAD inhibition method for neuroectodermal induction, combining the E-cadherin bioconjugates (inhibiting SMAD2/3) with Noggin (inhibiting SMAD1/5/8). Under these conditions, expression of neuroectodermal markers *PAX6* and *FOXG1* increased markedly. Importantly, applying a low-intensity oscillating magnetic field using a custom-built device, piconewton-scale forces were generated through the bioconjugates and produced even stronger *PAX6* and *FOXG1* upregulation. Collectively, these findings demonstrate that E-cadherin stimulation by MNPs can coordinately modulate Hippo and TGF-ß signaling to direct iPSC differentiation toward neuroectoderm. This magnetically responsive platform offers remote, tunable control of cell fate and opens promising avenues for mechanically driven biological applications.

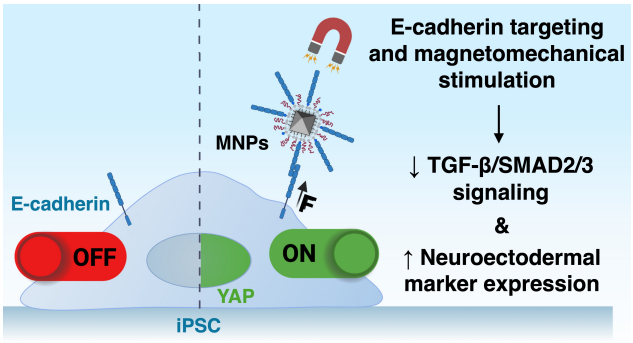

Figure 1: Overview of E-cadherin targeting and stimulation effects in iPSCs

Overview of e-cadherin targeting and stimulation effects in ipscs.jpg

Engineering inhalable siRNA polyplexes for the treatment of interstitial lung diseases

Friday, 16th January - 14:46: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 262

Leon Reger [1], ***Simone Carneiro*** [1], ***Daniela Pizzirani*** [2], ***Olivia M. Merkel*** [3]

1. *Ludwig-Maximilians-Universität München, Department of Pharmacy, Butenandstr. 5-13, 81377 Munich, Germany,* ***2.*** *Chiesi Farmaceutici S.p.A., Largo Belloli 11/A - 43122 Parma, Italy,* ***3.*** *Ludwig-Maximilians-Universität München, Department of Pharmacy, Butenandstr. 5-13, 81377; Munich, Germany;Ludwig-Maximilians-University Munich, Member of the German Center for Lung Research (DZL)*

Introduction:

Small interfering RNA (siRNA) offers a great platform for developing new therapeutics targeting a broad spectrum of diseases, including interstitial lung diseases (ILDs), a heterogeneous group of chronic respiratory disorders. Because of their negative charge and size, siRNA cannot passively cross cell membranes. Polyplex-based delivery systems address these barriers by protecting siRNA and facilitating intracellular uptake via endocytosis. Local pulmonary delivery of polyplexes offers promise for ILDs. In this study, we tested our platform against a biological target relevant to ILDs to achieve efficient lung delivery.

Methods:

We used a spermine-based polyacrylamide with a hydrophobic side chain to deliver siRNA. Polyplexes were prepared at five-fold and seven-fold nitrogen to phosphate (N/P) ratios and characterized for encapsulation efficiency, hydrodynamic diameter, polydispersity index (PDI), and zeta potential by dynamic/electrophoretic light scattering (Zetasizer Ultra, Malvern Instruments, UK). Target knockdown was quantified by qPCR in *in vitro* submerged cultures of murine fibroblasts (L929) and human lung epithelial cells (A549). Specificity was evaluated using scrambled negative-control siRNA and GAPDH-targeting siRNA. Cytotoxicity was assessed by LDH release and CellTiter-Glo®. Air–liquid interface (ALI) cultures of 16HBE14o- bronchial epithelial cells modeled airway delivery. For inhalation translation, DNA-surrogate–containing polyplexes were spray-dried with 5% trehalose; residual moisture and post-reconstitution particle size were measured.

Results:

At N/P 5 and 7, polyplexes showed high encapsulation efficiency, hydrodynamic diameters <150 nm, slightly positive zeta potentials, and PDIs <0.2. *In vitro* submerged L929 and A549 cultures, target-specific siRNA polyplexes mediated robust, sequence-selective knockdown exceeding 70% by qPCR with minimal off-target signal. In 16HBE14o-ALI cultures, N/P 7 achieved >50% reduction of target expression. LDH and CellTiter-Glo® indicated >70% viability across N/P ratios and siRNAs. Spray-drying produced free-flowing powders with residual moisture <3%; upon reconstitution, particle size was retained, indicating preserved colloidal stability.

Discussion:

These findings support an inhalable, well-tolerated siRNA polyplex platform for respiratory indications within ILD. The formulation combines favorable nanoscale properties, activity in airway-relevant models, and conver-

sion to a stable, reconstitutable dry powder for pulmonary delivery. Next steps include aerosol performance and lung-deposition studies and safety and efficacy evaluation in fibrotic *in vivo* models.

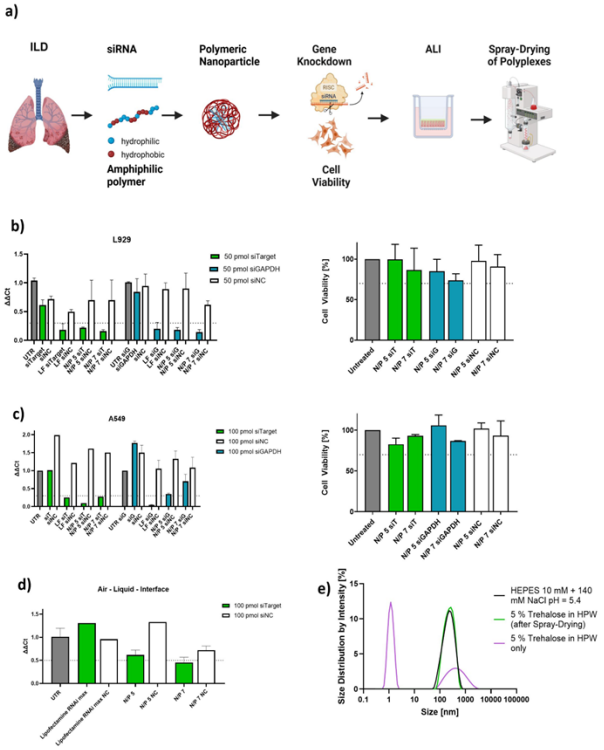

Figure 1 – Schematic workflow illustration (a); *in vitro* downregulation activity of siRNA polyplexes after 48 h of incubation and cytocompatibility assessment after 24 h in L929 cells (b) and A549 cells (c); *in vitro* downregulation activity of siRNA polyplexes after 48 h of incubation in air–liquid interface (ALI) culture of 16HBE14o- bronchial epithelial cells (d); size [nm] of DNA-polyplexes before (black) and after spray-drying (green) (e).

Figure1.c.png

Mirror-Image Peptides for Nucleic Acid Delivery: Toward Stable and Tunable Nanocarriers

Friday, 16th January - 15:02: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 67

Lucia Salvioni [1], ***Andrea Banfi*** [1], ***Davide Prosperi*** [1]

1. *University of Milan Bicocca*

The development of efficient delivery systems for nucleic acid (NA)-based therapies is an ongoing challenge. Lipid-based nanoparticles are widely used; however, they present limitations, including poor specificity, toxicity, and instability under physiological conditions. Peptide-based systems are emerging as promising alternatives due to their tunable properties. Nevertheless, their clinical application is hindered by their susceptibility to proteases and limited stability.

In this project, we investigate the potential of mirror-image peptides (MIPs) - synthetic peptides composed exclusively of D-amino acids - as nanovectors for NA delivery. Due to their inverted chirality, D-peptides demonstrate remarkable resistance to protease activity while retaining biological functionality.

Among various constructs, we selected RALA, a promising 30-amino acid cell-penetrating sequence that, due to its charged residues, self-assembles upon interaction with negatively charged NAs. Using both manual and automated microfluidic-based synthesis, we produced nanoparticles complexed with either RNA or double-stranded DNA. Our study focuses on three molecular forms of the RALA peptide: one composed entirely of L-amino acids, another composed of D-amino acids, and a *retro-inverso* form, which consists of D-amino acids arranged in a reverse sequence. This design enables us to investigate how peptide chirality and sequence orientation influence the structural properties and delivery efficiency of the resulting NA-loaded nanoparticles.

Our results demonstrate that microfluidics synthesis ensures superior size control compared to manual methods and, importantly, offers a scalable and reproducible platform suitable for future clinical translation. The obtained nanoparticles were evaluated for their stability in serum and protease-resistance through gel electrophoresis, which revealed significantly enhanced retention of NA cargo in D-form nanoparticles relative to their natural L-form counterparts.

Functional *in vitro* validation through luciferase silencing assays showed that MIPs-based nanoparticles efficiently deliver siRNA with minimal cytotoxicity. Notably, microfluidic-generated D-RALA NPs outperformed their manually synthesized counterparts, highlighting the impact of the complexation method on gene silencing efficiency and overall nanoparticle activity.

This work lays the foundation for the development of next-generation MIPs-based nanoparticles as effective, biocompatible and scalable vectors for NA delivery. Future studies will leverage the chemical versatility of peptides to explore targeted strategies, further advancing the design of tunable carriers for NA therapeutics.

Extracellular vesicles predict recovery after rehabilitation in stroke survivors: application of a multiplexing SPRi based biosensor

Friday, 16th January - 15:18: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 244

Aurora Mangolini [1], Silvia Picciolini [1], Pietro Arcuri [1], Donata Bardi [2], Leonardo Cosco [2], Francesca Cecchi [2], Lorenzo Romagnoli [2], Ester Marra [2], Pietro Parisse [3], Andrea Mannini [2], Jorge Navarro [1], Marzia Bedoni [1], Alice Gualerzi [1]

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In those who survive cerebral stroke, inflammation has a detrimental time-dependent role, perpetuating the injury, but also a protective action promoting tissue regeneration. Timely intensive rehabilitation is crucial to contrast the negative escalation of the events that follow a stroke injury and to favor a positive niche for the regeneration of damaged tissue and the restoration of physiological function.

The aim of the present study was the application of a multiplexed biosensor for the identification of measurable blood biomarkers associated to Extracellular Vesicles (EVs) that could be predictive of functional recovery in stroke survivors.

EVs are natural nanoparticles that mediate long distance intercellular communications. They can be detected in blood and other biofluids thanks to ultrasensitive techniques. Following the EXO4STROKE protocol (ClinicalTrials ID: NCT05370105), 30 stroke patients in sub-acute phase were enrolled. EVs were isolated by size exclusion chromatography in the serum of patients at admission (T0) and at discharge (T1) in intensive rehabilitation unit (Figure 1A). Taking advantage of an optimized biosensor, the Surface Plasmon Resonance imaging (SPRi) technique was exploited to obtain a multiplexed analysis of circulating EVs from brain (neurons, astrocytes, microglia) and non-brain (endothelium, skeletal muscle and platelets) cells (Figure 1B), and for the relative quantification of markers of pathological or regenerative processes. Machine learning-based analysis complemented the study by integrating statistically significant features in a cross-validated prediction model targeting functional recovery (modified Barthel Index) at T1 from T0 data.

In the considered cohort, elevated circulating levels of EVs from neurons (CD171+) and microglia (CD11b+), 2-4 weeks after the stroke event, were associated with better recovery at 2 months. Moreover, the overexpression of the VEGF receptor on microglial EVs (IB4+ and CD11b+), was associated with higher functional improvement. Alternatively, the overexpression of TGF-β receptor on IB4+ EVs during the subacute phase post-stroke was found associated with increased stroke severity.

The major finding of the present study is the successful application of a multiplexing SPRi-biosensor for the identification of a small panel of biomarkers associated to circulating EVs that can objectively assess the neuroinflammatory status of stroke patients and predict their functional recovery after rehabilitation.

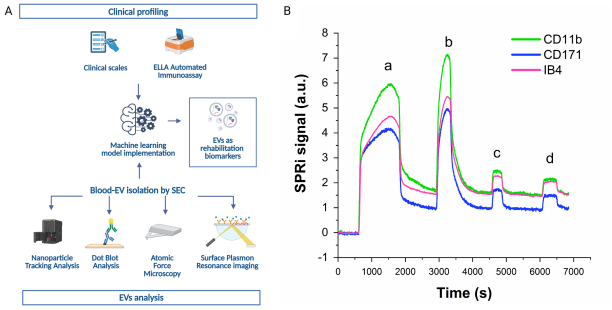

Figure 1. A) Schematic representation of the study activities describing the multidisciplinary approach. B) SPRi sensorgram obtained by the injection of blood-derived extracellular vesicles (EVs) on a functionalized multiplexing biosensor. 'a' indicates the binding of EVs on the surface of the SPRi biochip, 'b-d' indicate subsequent injections of secondary analytes for the double labelling of EVs.

Figure1.png

Towards “Autonomous” Minimal Cells as Next-Gen Therapeutics

Friday, 16th January - 15:34: Diagnostics and Devices (Room 1) - Oral - Abstract ID: 173

Simone Giaveri [1]

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Recent advances in the engineering of cell-free systems with integrated biomimetic functions have enabled the development of sophisticated cell mimics for therapeutic applications, including tissue angiogenesis and vasodilation. To date, however, the majority of such cell-free systems are programmed to release therapeutics that are synthesised *in situ*, by using provided precursors. Recently I took inspiration from the way nature operates tightly integrated metabolic and genetic networks for engineering a cell-free system that is capable to self-sustain autonomously using CO_2, by simultaneously deploying 53 enzymes recruited from across all domains of life. Building on this transformative achievement, and its demonstrated feasibility, I now seek to explore its potential for the bottom-up engineering of advanced therapeutic platforms.

Light-Based 3D Printing of Biodegradable Functional Devices

Friday, 16th January - 15:50: Diagnostics and Devices (Room 1) - Invited Speaker - Abstract ID: 324

Yinyin Bao [1]

1. *University of Helsinki*

3D printing, with its revolutionary digital fabrication methods, has brought tremendous impact on numerous fields including energy and chemical engineering, soft robotics, and biomedicine. Due to its high printing resolution, fast printing process, and flexibility in material design, light-based 3D printing methods—especially digital light processing (DLP)—has attracted widespread interest and shown enormous potential in personalized medicine and drug delivery systems.[1,2] However, biocompatible and biodegradable materials available for these technologies that can provide excellent mechanical properties are still limited. Commonly used printing materials typically utilize oligomers and a large amount of diluents to prepare photopolymerizable resins to meet required printing parameters, and their comprehensive performance is difficult to meet practical application needs. This presentation will focus on the macromolecular design and engineering involving biodegradable photopolymers and functional nanomaterials, to facilitate the application of light-based 3D printing in personalized medical devices, bioactive scaffolds, and drug delivery systems.[3-5]

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