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# II PASSION FOR SCIENCE Congress

13th | November | 2025
FACULTY OF PHARMACY. UNIVERSITY OF THE BASQUE COUNTRY (EHU),
Álava Campus, Vitoria-Gasteiz.

**Organized by:**
"Aula de Medicina Personalizada EHU i+Med" Faculty of Pharmacy (EHU)

**Sponsored by:**
Vice-Rectorate for Scientific-Social Development and Transfer and "Aula de Medicina Personalizada EHU i+Med"

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**Organizing Committee:**

- Mirari Ayerbe (Dean of the Faculty of Pharmacy, EHU)
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II PASSION FOR SCIENCE Congress

# PROGRAMME 13th | November | 2025

## II 'PASSION FOR SCIENCE' CONGRESS

## Location: Faculty of Pharmacy Auditorium (EHU). Vitoria-Gasteiz

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| **08:30 - 09:00** | **Registration & Presentations uploading/poster placement**<br>Main hall of the Faculty of Pharmacy (EHU) |
| **09:00 - 09:15** | **Welcome session**<br>• **Joxerramon Bengoetxea** (Rector of the EHU)<br>• **Amaia Esquisabel** (Director of Science Policy for the Basque Government)<br>• **Mirari Ayerbe** (Dean of the Faculty of Pharmacy, EHU)<br>• **Sandra Benito** (Laboratory Manager and Member of the Governing Council of the Cooperative of i+Med)<br>• **Rosa Hernández** (Director of the Aula de Medicina Personalizada EHU i+Med) |
| **09:15 - 10:00** | **PLENARY SPEAKER I. *Chairperson: Nicolas Nazar*.**<br>• **Burcu Gumuscu-Sefunc.** Tenure-track assistant professor in the Department of Biomedical Engineering at Eindhoven University of Technology (TU/e): "Enhancing Digital Droplet Microfluidics for Cell Culture and Stimulation" |
| **10:00 - 10:45** | **Oral presentations. Session I. *Chairperson: Nicolas Nazar*.**<br>Selected talks: 7-minute presentation, 3 minutes for Q&A<br>• **Gema del Rocío López Buenafé.** Development of PEDOT: PSS-based Microstructured Electrodes for Bioelectronic Interfaces in Cancer Research<br>• **Ramon Roset Visiedo.** RNAzyme-Based Strategies for MicroRNA Detection in Forensic Applications<br>• **Sukayna Ezquerro Berdouzi.** Microfluidic fiber-optic LSPR sensor for VEGF detection in mesenchymal stem cell culture.<br>• **Naiara Lartitegui-Meneses.** Evaluation of PCSK6 expression and secretion in Testicular Germ Cell Tumors by immunohistochemistry and CellStudio platform |
| **10:45 - 11:30** | **Coffee break and Poster viewing** |
| **11:30 - 12:45** | **Flash poster presentations. *Chairperson: Saioa Gomez y Victor Carramiñana*.**<br>Make your research unforgettable: 1 poster, 3 minutes.<br>• **Mikel Salmeron.** Towards Reliable Preclinical Testing: Early-Stage Development of a Bioprinted 3D In Vitro Chronic Wound Model<br>• **Martina Gruppuso.** An in vitro model of human glioblastoma multiforme to study early-stage glioma progression in the tumour-associated microenvironment<br>• **Gesala Pérez.** Nutritional interventions in celiac disease: towards a holistic management and future challenges<br>• **Adrián Salazar.** Identification of novel genes potentially involved in the biofilm-forming ability of Arcobacter butzleri<br>• **Nerea Herran-Diaz de Argote.** Analytical techniques for identifying anthropogenic fire in Middle Pleistocene sediment samples<br>• **Eider Sustatxa.** Bioactive hydrogel coatings on titanium implant surface simulators<br>• **Laura Merino.** Development and characterization of heparin-loaded bioinks for 3D bioprinting of elastic tissue.<br>• **Beatriz Sáenz.** Pharmacological inhibition of mTOR improves hERG channel performance in a cellular model of LQTS2 |

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| **11:30 - 12:45** | • **Leyre López de Aguileta.** Synthesis of Nitrogen Heterocycles as Human Topoisomerase Inhibitors<br>• **Asier Inchaurraga Llamas.** Single-Cell Adhesion Dot Array (SCADA) enables high-resolution profiling of breast cancer cell–matrix interactions<br>• **Isabel Poves Ruiz.** A paper-based microfluidic device for the colorimetric detection of scopolamine with the naked eye.<br>• **Alberto Gamalier Casado-Cedano.** SLAMF3 Expression and Adhesion Dynamics of Jurkat Cells in Microfluidic Device.<br>• **Julie Matias Decuyper.** Development of dECM-Based Bioinks for 3D Bioprinting of Tendon Tissue |
| **12:45 - 13:30** | **Oral presentations. Session II. *Chairperson: Javier Vicario*.**<br>Selected talks: 7-minute presentation, 3 minutes for Q&A<br>• **Laura Arellano.** Effect of viable and inactivated Lactobacillus rhamnosus GG administration on the prevention of diet-induced obesity in rats: Implication of white and brown adipose tissue and influence of bacterial viability<br>• **Erik Barrio.** E3 ligase Ube3a targets mTOR for degradation<br>• **Angela Trejo.** Novel antiplasmodial compounds via sulfadoxine modification through multicomponent reactions<br>• **Alexander Mirandona-Olaeta.** Hybrid Metal–Organic Framework electrolytes for safer, high-energy rechargeable batteries |
| **13:30 - 14:30** | **Lunch Break** |
| **14:30 - 15:15** | **PLENARY SPEAKER II. *Chairperson: Edorta Santos*.**<br>• Eneko Larrañeta. Chair in Pharmaceutical Materials Science. Queen´s University of Belfast: “Advanced Implantable Platforms for Sustained Drug Administration” |
| **15:15 - 16:00** | **Oral presentations. Session III. *Chairperson: Edorta Santos*.**<br>Selected talks: 7-minute presentation, 3 minutes for Q&A<br>• **Maria Rossello-Gelabert.** Prime-LS, a cryoprotectant-free lyophilized MSC-secretome providing complete protection against ulcerative colitis<br>• **Madalen Arribas Galarreta.** Identification of novel antibodies against the ultraconserved MPER region of SARS-CoV-2 by phage display<br>• **Deepti Rana.** Dynamic Biomaterials for Vascularized Engineered Tissues<br>• **Leire Berasategi Asurmendi.** Analysis of Protein Delivery Efficiency using GFP- and Luciferase-Loaded Extracellular Vesicles |
| **16:00 - 16:45** | **Experiences beyond the Academy**<br>• Amaia Huguet. I+Med Director of R&D Operations<br>• Susana Egusquiaguirre. Patent Adviser. ABG Intellectual Property<br>• Enara Herrán. Chief Executive Officer of Additum Valoren Salud<br>• Pablo Ortiz. Venture Builder at Tecnalia |

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| **16:45 - 17:30** | **Oral presentations. Session IV. *Chairperson: Edorta Santos*.**<br>Selected talks: 7-minute presentation, 3 minutes for Q&A<br>• **Nekane Martin Mendia.** Mucoadhesive Nanoparticles Based on Chitosan Derivatives for Enhanced Ophthalmic Drug Delivery<br>• **Ainhoa Goenaga.** Dual Targeting of Wnt Signaling and DR5 Activation for Tumor Therapy<br>• **Paula Fernández Muro.** Complement factor H gene supplementation therapy for dry age-related macular degeneration<br>• **Camino Garcia-Blasco.** Development of a colon-targeted delivery system for mesenchymal stromal cell-derived secretome in inflammatory bowel disease |
| **17:30 - 18:15** | **Coffee-break and Poster Viewing** |
| **18:15** | **Closing Remarks and Award Ceremony** |

# POSTERS LIST

**"Posters selected for Flash Poster Presentations will also be presented during Poster Sessions"**

1. **Mikel Salmeron.** Towards Reliable Preclinical Testing: Early-Stage Development of a Bioprinted 3D In Vitro Chronic Wound Model
2. **Martina Gruppuso.** An in vitro model of human glioblastoma multiforme to study early-stage glioma progression in the tumour-associated microenvironment
3. **Gesala Pérez.** Nutritional interventions in celiac disease: towards a holistic management and future challenges
4. **Adrián Salazar.** Identification of novel genes potentially involved in the biofilm-forming ability of Arcobacter butzleri
5. **Nerea Herran-Diaz de Argote.** Analytical techniques for identifying anthropogenic fire in Midd- le Pleistocene sediment samples
6. **Eider Sustatxa.** Bioactive hydrogel coatings on titanium implant surface simulators
7. **Laura Merino Fernández**. Development and characterization of heparin-loaded bioinks for 3D bioprinting of elastic tissue.
8. **Susana Abrante.** Stability of added gamma-oryzanol during sunflower oil heating at frying tem- peratures: kinetics and degradation products
9. **Beatriz Sáenz.** Pharmacological inhibition of mTOR improves hERG channel performance in a cellular model of LQTS2
10. **Irene Diez Aldama.** 3D bioprinted vascular constructs with ECM-mimetic properties: Functional and structural analysis.
11. **Leyre López de Aguileta.** Synthesis of Nitrogen Heterocycles as Human Topoisomerase Inhibitor
12. **Asier Inchaurraga Llamas.** Single-Cell Adhesion Dot Array (SCADA) enables high-resolution profiling of breast cancer cell–matrix interactions
13. **Isabel Poves Ruiz.** A paper-based microfluidic device for the colorimetric detection of scopola- mine with the naked eye.
14. **Alberto Gamalier Casado-Cedano.** SLAMF3 Expression and Adhesion Dynamics of Jurkat Cells in Microfluidic Device.

**15. Julie Matias Decuyper.** Development of dECM-Based Bioinks for 3D Bioprinting of Tendon Tissue

**16. Marie J. Gouteron.** [6]- and [7]-Helicenic Diols as Scaffolds for the Synthesis of a New family of Chiral Brønsted Acids

**17. Lourdes Basabe-Desmonts.** Generation and combination of ionogel microstructures using vacuum-driven lithography technique

**18. Nahia Ureña Esteban.** Isolation, identification, and characterization of bacteriophages for the elimination of Staphylococcus aureus

**19. Helen Carr.** Sexual dimorphism in the treatment of rats with Opuntia strica var. dillenii fruit extract to prevent obesity and related co-morbidities

**20. Irene Besné-Eseverri.** Preventive effect of Opuntia extracts in steatosis and autophagy in a murine model of diet-induced liver disease

**21. Oier Encinas.** Development of hydrogen sulphide-activated theragnostic prodrugs for selective cancer treatment through tetrazine dynamic chemistry

**22. Alejandro Serrano.** Design of Treg-targeted nanoparticles for cancer treatment

**23. Elena Valgañón.** Evaluation of biosurfactant-producing halophilic bacteria for the bioremediation of oil-contaminated sands

**24. Zuriñe Eraña.** Extracellular Vesicles as Biologic Drug Delivery Systems: Pharmacokinetic Advantages over Soluble Forms

**25. Ana Alarcia.** Population pharmacokinetic modeling of piperacillin administered as extended infusion in critically ill patients

**26. P. E. Guevara-Pantoja.** Autonomous paper valves using pdms vacuum pumps as actuators for colorimetric chrono-sampling.

## KEY DATES

- 30th September 2025 | Closing of submission period
- 20th October 2025 | Notification of acceptance of communications

## INFORMATION ABOUT AWARDS*

- Oral communications: two prizes of €1000 each for participation in congresses of the winner's choice.
- Posters: two €300 Elkar gift cards for the best two flash poster presentations.

* Only PhD students who have not defended their thesis by the date of the congress will be eligible for the awards

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# PLENARY SPEAKERS

## ABOUT THE SPEAKERS

# Dr. Burcu Gumuscu-Sefunc

**Dr. Burcu Gumuscu-Sefunc is an assistant professor at the Biomedical Engineering department in Eindhoven University of Technology,** where she leads Biosensors and Devices group.

**She is a pioneer of hydrogel micropatterned surfaces** via capillary pinning and protein-barcoded hydrogel microparticles for single cell analysis.

**More recently she focuses on developing digital microfluidic platforms** to study cell-biomaterial interactions for long-term experiments.

**Gumuscu-Sefunc received prestigious awards and grants** from Royal Dutch Academy of Science, Dutch Research Council, and European Commision.

**She is an advisory board member at Lab on a Chip Journal,** and editorial board member at Micromachines, Frontiers in Digital Health and Frontiers in Lab on a Chip Technologies Journals.

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# Digital Droplet Microfluidics for Cell Culture and Stimulation

B. Gumuscu[1]*

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**Abstract**

Unlike conventional microfluidic systems that rely on continuous flow through fixed channels, Digital microfluidics (DMF) chips are designed with arrays of millimeter-scale electrodes. By applying controlled voltages to these electrodes via electro-wetting based approach, sub-microliter droplets can be precisely actuated to move, merge, split, and mix across the chip surface. Such capabilities enabled the automation of a wide range of labor-intensive biological and chemical assays. In addition to these, a particularly exciting and emerging application is the modulation of cell behavior using electric fields. DMF platforms can generate spatially and temporally controlled electric fields at the microscale, enabling new ways to influence cell adhesion, migration, morphology, and even differentiation. This adds a powerful bioelectric layer of control to cellular assays, especially valuable in studying electroresponsive cell types or developing bioelectronic interfaces.

Despite these advancements, several technical limitations continue to constrain the broader implementation of DMF systems in biological research and clinical diagnostics. Two key challenges stand out. First, the planar, two-dimensional nature of current DMF chip designs restricts the number of operational units that can be integrated on a single device, thereby limiting the ability to perform highly multiplexed or parallelized assays. Second, the compatibility of DMF devices with long-term cell culture remains problematic. The electronic components typically used in DMF chips are not well-suited for the humid, temperature-controlled environments required for extended biological experiments, such as those inside standard $CO_2$ incubators.

We explore these challenges in detail and outline a set of potential engineering and materials-based solutions aimed at extending the functional range of DMF chips (*Fig. 1*). These include design innovations for three-dimensional electrode architectures to increase operational density, and the development of robust encapsulation methods to enhance the environmental stability of electronic components under biological conditions. By addressing these challenges, we can unlock new potential for DMF-based platforms—not only for automated biochemical assays but also for the active modulation of living systems through precisely applied electric fields.

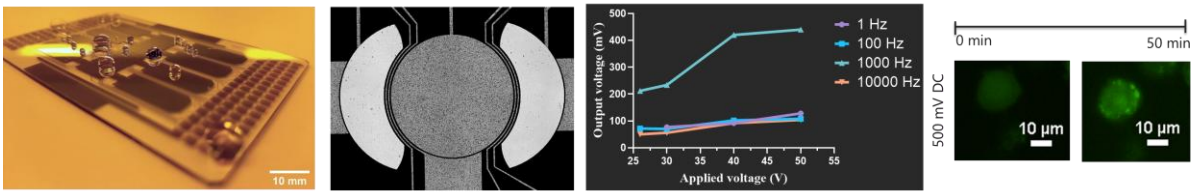


*Fig 1*. DMF device and its use in electrical modulation in long-term macrophage cultures.

**Acknowledgments**

The author acknowledges the support and discussions in the Biosensors and Devices Lab at the Eindhoven University of Technology.

**References**

[1] B.B. Li, et al., Cell invasion in digital microfluidic microgel systems, Sci. Adv. 6 (2020) 26.

[2] X. Xu, et al., Digital microfluidics for biological analysis and applications, Lab Chip 23 (2023) 1169–1191.

[3] A.H.C. Ng, et al., Digital microfluidics cell culture, Annu. Rev. Biomed. Eng. 17 (2015) 91–112.

[4] O.K. Savchak, B. Gumuscu, Long-term digital microfluidic chips for regulating macrophage cellular interactions in inflammation, Lab Chip 25 (2024) 7.

# Eneko Larrañeta

**Eneko Larrañeta is a Professor at Queen's University Belfast,** specialising in drug delivery systems and biomaterials.

**He holds a BSc in Chemistry and a PhD in Physical Chemistry from the University of Navarra,** where his research focused on self-assembled hydrogels. After completing his PhD in 2012, Prof. Larrañeta worked as a research fellow in nanotechnology for drug delivery before moving to Belfast in 2013 to develop microneedle technology for transdermal drug delivery at Queen's University Belfast.

**Prof. Larrañeta's expertise includes hydrogels, nano/microparticles, and microneedle-based systems.** Currently, he focuses on implantable systems for sustained drug release, using techniques such as melt processing and additive manufacturing. He has published over 100 papers in peer-reviewed journals, edited multiple books, and authored numerous book chapters. Prof. Larrañeta has secured funding from leading organisations and collaborated extensively with pharmaceutical and cosmetics companies.

**In 2023, he was named a Clarivate Highly Cited Researcher,** and since 2019, he has been recognised as a top 2% scientist in his field by Stanford University's analysis using Scopus data. He is a Fellow of the UK Higher Education Academy and a member of the Royal Society of Chemistry and the Society for Applied Microbiology.

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# Advanced Implantable Platforms for Sustained Drug Administration

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## Abstract

Implantable drug delivery systems (IDDS) represent a promising alternative to conventional routes of drug administration [1]. Oral and injectable delivery methods, while common, typically result in fluctuating drug concentrations, characterised by an initial peak in blood levels followed by a rapid decline, necessitating frequent dosing to maintain therapeutic levels. Oral delivery also faces challenges such as drug degradation in the gastrointestinal tract and first-pass metabolism, which can reduce drug efficacy [2]. In contrast, IDDS can provide sustained, controlled drug release over extended periods, making them particularly beneficial for managing chronic conditions where patient adherence to regular dosing is often problematic [3]. Although traditionally used for systemic delivery, implantable systems are increasingly being explored for localised administration. This approach can enhance drug concentrations at the target site while minimising systemic exposure and associated side effects [2]. This talk will explore a range of implantable systems developed for sustained drug delivery, with a focus on their relevance to chronic disease management. It will present results from implants manufactured using 3D printing techniques, such as fused deposition modelling and stereolithography, as well as melt processing and direct compression methods. Additionally, the development of porous membranes and biodegradable coatings designed to prolong drug release will be discussed. The presentation will cover the design, characterisation, and application of various implantable devices, highlighting how these technologies enable personalised treatment strategies. By ensuring precise, localised, and long-acting drug administration, these systems offer improved therapeutic outcomes and reduced side effects.

## References

[1] Quarterman JC, Geary SM, Salem AK. Evolution of drug-eluting biomedical implants for sustained drug delivery. European Journal of Pharmaceutics and Biopharmaceutics 2021;159:21–35. https://doi.org/10.1016/j.ejpb.2020.12.005.

[2] Magill E, Demartis S, Gavini E, Permana AD, Thakur RRS, Adrianto MF, et al. Solid implantable devices for sustained drug delivery. Adv Drug Deliv Rev 2023;199:114950. https://doi.org/10.1016/j.addr.2023.114950.

[3] Corduas F, Mancuso E, Lamprou DA. Long-acting implantable devices for the prevention and personalised treatment of infectious, inflammatory and chronic diseases. J Drug Deliv Sci Technol 2020;60:101952. https://doi.org/https://doi.org/10.1016/j.jddst.2020.101952.

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# EXPERIENCES BEYOND THE ACADEMY

# Amaia Huguet

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**Amaia Huguet Casquero is the Director of R&D Operations at i+Med,** with extensive expertise in project management and scientific innovation. She obtained her PhD Cum Laude in Pharmaceutical Technology from the University of the Basque Country (EHU) in 2020, following a Master's in Research, Development, and Innovation of Medicines from the University of Navarra (2015) and a Degree in Pharmacy from EHU (2014).

**Her academic training is further strengthened by specialized qualifications in drug development, Good Manufacturing Practices (GMP), and project and innovation management.**

**Dr. Huguet-Casquero began her professional career as R&D Technical Manager at BIOSASUN,** before moving on to lead Project Management at Unikare Bioscience. Since 2023, she has served as Director of R&D Operations at i+Med.

**At i+Med, she currently focuses on leading the project management team** in securing R&D&I funding, supervising the technical and financial monitoring of projects, coordinating the preparation and submission of competitive national and European research proposals, and spearheading the creation of a new research institute. She is also responsible for fostering strategic collaborations with technology centers, leading universities, physicians, and other professionals across the healthcare sector.

**Throughout her career, she has contributed to over 40 public and private R&D projects** in areas such as wound healing, 3D bioprinting, bioelectronic sensors, controlled drug release, and nanotechnology, and has authored six high-impact scientific publications.

# Susana Egusquiaguirre

**Susana Egusquiaguirre is a Patent Adviser in Biotechnology and Life Sciences at ABG Intellectual Property.** Her practice is focused on patent drafting, prosecution, and opinion work, particularly in relation to molecular and cellular biology, pharmacogenomics, gene therapy, immunology, animal models, and diagnostic methods.

**Before joining ABG IP, Susana worked as a Clinical Research Scientist** and as an Intellectual Property Counsel in the pharmaceutical industry. Her responsibilities included patentability identification and evaluation of the company's discoveries, preparation of freedom-to-operate reports and due diligence, or acting as a consultant on patent drafting and prosecution.

**Susana holds a Degree in Pharmacy and a PhD in Pharmacy from the University of the Basque Country,** at the NanoBioCel Group, where her research focused on the development of nanoparticles encapsulating bioactive peptides or pharmaceutical agents to recover telomerase activity.

**During her PhD she did research stays at the Neurodegenerative Diseases unit of the Instituto de Investigación Hospital 12 de Octubre (Madrid),** at the Institute for Biological and Medical Imaging (IBMI) of the Helmholtz Zentrum München (Munich), and at the Instituto de Investigaciones Biomédicas Sols-Morreale (Madrid).

**After completing her PhD, Susana worked at Dana-Farber Cancer Institute-Harvard Medical School (Boston),** where she studied the pathogenic roles of oncogenic transcription factor STAT3 target genes.

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# Enara Herrán Martínez

**LinkedIn:** (48) Enara Herran Martinez | LinkedIn

**Enara Herrán Martínez is Project Area Director at Additum – Valor en Salud,** where she specialises in developing new healthcare models aimed at significantly improving the efficiency of care processes within the healthcare system.

**She holds a Bachelor's degree in Pharmacy, two Master's degrees** (in Pharmacology and in Clinical Research), and a PhD in Pharmacy from the University of the Basque Country, where her doctoral thesis focused on the development of micro- and nanoparticles as therapeutic tools for neurodegenerative diseases.

**After completing her PhD in 2014, Dr. Herrán worked as a researcher and project coordinator in various institutions,** including the University of the Basque Country, Biopraxis Research AIE, and the Biokeralty Research Institute, leading initiatives focused on chronic and neurodegenerative diseases.

**Currently, her work at Additum is centred on designing new value-based healthcare models** that integrate innovative digital technologies to optimise process efficiency and facilitate access to preventive, predictive, and personalised medicine.

**She has led over 20 healthcare innovation projects,** secured regional and European funding (including H2020, CDTI, and EIT Health), and actively collaborates with academic, clinical, and industrial stakeholders.

**Dr. Herrán is the author of 17 scientific publications,** holds a patent and an industrial secret, and remains strongly committed to improving patient health through innovative, technology-driven healthcare solutions.

# Pablo Ortiz

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**Pablo Ortiz graduated with honors in Pharmacy from the University of the Basque Country (2012).** He then obtained a Master's degree in Synthetic and Industrial Chemistry from the University of the Basque Country (2013).

**After that, he moved to the Netherlands, where he obtained his PhD in Organic Chemistry from the University of Groningen (2017).** That same year, he joined VITO (Belgian Institute for Technological Research), first as a postdoc and then as a researcher. He helped establish the biopolymer development group and was responsible for establishing and managing the VITO satellite laboratory at the Green Chemistry Campus (Netherlands).

**In 2020, he joined Tecnalia as a project manager in the field of bio-based materials and CO2 capture and uses.**

**In 2023, he earned an MBA from the Open University of Catalonia.** That same year, he was appointed to the board of directors of the European association promoting CO2 capture and utilization technologies, CO2 Value Europe.

**He is a co-author of more than 25 scientific articles and six patents.** Since 2025, he is a Venture Builder at Tecnalia, transferring the technology developed at the center to the market by creating new companies and businesses.

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## ORAL COMUNICATIONS
## Session I

# Development of PEDOT:PSS-based Microstructured Electrodes for Bioelectronic Interfaces in Cancer Research

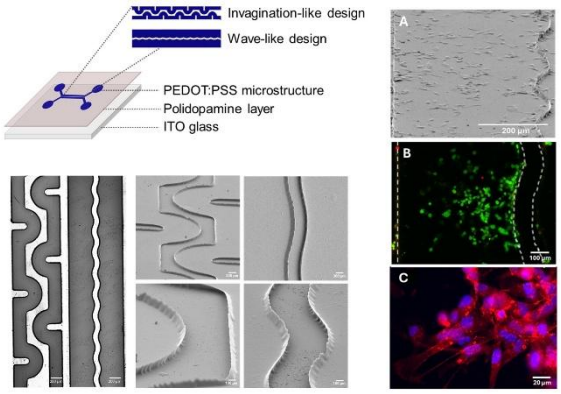
Gema del Rocio Lopez-Buenafe[1], Juncal Anne Alonso-Cabrera[1], Carlos Marcuello[3], Maider Ortiz-Perez[3], Fernando Benito-Lopez[1], Adai Colom[3,4], Lourdes Basabe-Desmonts[1,4] and Janire Saez[2,4]

[1] Microfluidics Cluster UPV/EHU, University of the Basque Country, SPAIN, [2] Zoology and Animal Cell Biology, University of the Basque Country, SPAIN, [3] Biofisika Institute (CSIC, UPV/EHU), University of the Basque Country, SPAIN, [4] Basque Foundation for Science, IKERBASQUE, SPAIN

Reliable *in vitro* platforms are crucial for cancer research, enabling controlled studies of tumor progression and therapy response. Bioelectronics offers real-time monitoring of cancer cell behavior by integrating cells with functional sensing.[1] Conductive polymers like PEDOT:PSS are promising for biocompatible, electrically active interfaces, but conventional fabrication requires costly, complex cleanroom processes.[2] Here, we demonstrate for the first time the use of vacuum soft lithography (VSL) to fabricate PEDOT:PSS microstructured electrodes, providing a scalable and accessible platform for breast cancer tumor monitoring.[3]

PEDOT:PSS microstructured electrodes were fabricated on ITO substrates via vacuum-assisted deposition through PDMS molds, using polydopamine for adhesion and dual-phase annealing for stability. Morphology was characterized by profilometry, SEM, and AFM, while EIS assessed electrical performance. Biocompatibility was tested with MDA-MB-231 cells cultured for 5 days. The electrodes exhibited precise replication of microchannel geometries, stable morphology, and hydration-dependent mechanical properties (Young's modulus from 2.9 to 0.9 MPa). AFM confirmed consistent surface roughness. EIS revealed that 2% GOPS provided optimal electrical behavior, with low impedance and balanced capacitive–resistive response. Cell viability assays and fluorescence/SEM imaging showed healthy, adherent, and organized cells, validating the platform's stability, electrical functionality, and biocompatibility for bioelectronic and tumor modeling applications.

This study demonstrates the fabrication of PEDOT:PSS-based microstructured electrodes via VSL and their biological and electrical suitability, establishing them as viable *in vitro* platforms for cancer research. This low-cost, scalable approach overcomes limitations of conventional fabrication while supporting cancer cell culture and enabling integration of bioelectronic sensing. These features position the system as a promising tool for modeling tumor microenvironments and real-time analysis of cancer cell behavior.

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# RNAzyme-Based Strategies for MicroRNA Detection in Forensic Applications.

Ramon Roset[1], F. Nicolas Nazar*[1], Lourdes Basabe-Desmonts[1,2], and Fernando Benito-Lopez[1]

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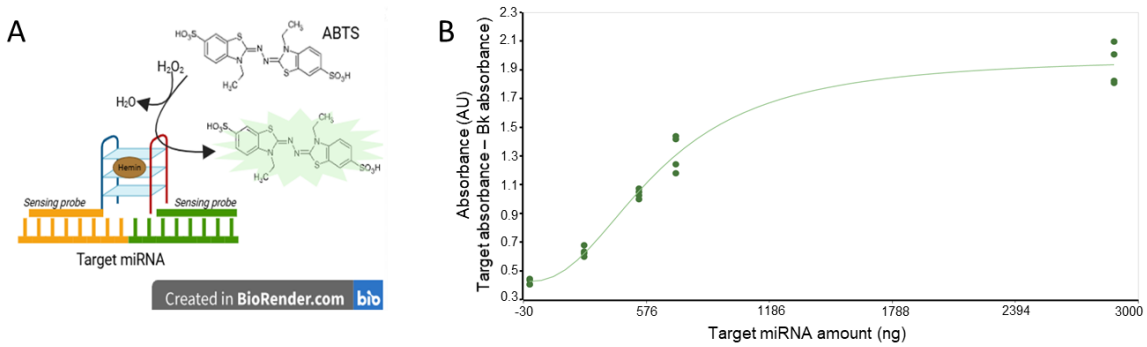
## Abstract

Accurate estimation of the post-mortem interval (PMI) is crucial in forensic investigations; however, current methods are mainly restricted to the early stages after death and are strongly affected by environmental and individual variability, or demand high levels of expertise and time, i.e., RT-PCR. MicroRNAs (miRNAs) have recently emerged as promising PMI biomarkers due to their stability against enzymatic degradation and decomposition [1]. RNAzymes, catalytic RNA-based systems, can be fine-tuned to bind specific microRNA sequences and produce a colorimetric signal through ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) oxidation, enabling specific detection and quantification [2],[3]. In this work, we present an RNAzyme-based sensor for the detection and quantification of a cardiac tissue miRNA, a biomarker whose levels decrease progressively after death [4]. RNAzyme sensing probes (SP) were designed to specifically recognize target miRNA and generate a colorimetric signal through ABTS oxidation. The system was optimized, showing activation by increasing target concentrations, with a calibration curve done at 22.5 min. The sensor also demonstrated high specificity, showing no signal increase when exposed to non-complementary miRNAs. These findings introduce a rapid, low-cost alternative to conventional forensic techniques.

**Keywords:** Post-mortem interval (PMI) estimation, RNAzyme, microRNA (miRNA), forensic science.

## Graphical abstract:




***RNAzyme-based system for PMI estimation.*** *A) Schematic representation of RNAzyme system functioning. B) Calibration curve of target miRNA-206 at 22.5 min ($R^2$=0.991), n=4.*

## Acknowledgments

This work was supported by Basque government, under grupos consolidados (Grant No IT1633-22), PREDESTOM under grant TED2021-129273B-C33 and MINECO under grant PID2020-120313GB-100, both funded by the Ministry of Science and Innovation of Spain through the State Research Agency (MCIN/AEI/10.13039/501100011033).

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# Microfluidic fiber-optic LSPR sensor for VEGF detection in mesenchymal stem cell culture

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**Abstract**

We report a fiber optic immunosensor integrated into a microfluidic device for the detection of vascular endothelial growth factor (VEGF) using localized surface plasmon resonance (LSPR) and gold nanoparticles (AuNPs). VEGF is a critical biomarker highly overexpressed in various cancers that plays a key angiogenic role [1]. Combining a multimode optical fiber integrated in a PMMA/PSA microfluidic device (Figure 1), the system enabled continuous flow and detection of the protein using a small sample volume. Under flow conditions, the time of detection was set at 2 min and the calibration curve was obtained. The platform enables optical quantification with automated microfluidics and minimal sample consumption, detecting as few as 1.8 × $10^4$ AuNPs on a 105 µm multimode fiber core [2]. As a proof of concept, the biosensing system detected and quantified VEGF in a concentrated supernatant of a 7-day mesenchymal stem cell (MSC) culture. MSCs are key in biomedical applications and secrete VEGF [3], supporting their relevance as the selected model system for validating our biosensor's performance. These results show the potential for rapid, quantitative, and miniaturized biomarker analysis in point-of-care applications.

**Keywords:** Optical microfluidic biosensor, Fiber optics, Sandwich immunoassay, Gold nanoparticles.

**Graphical abstract:**

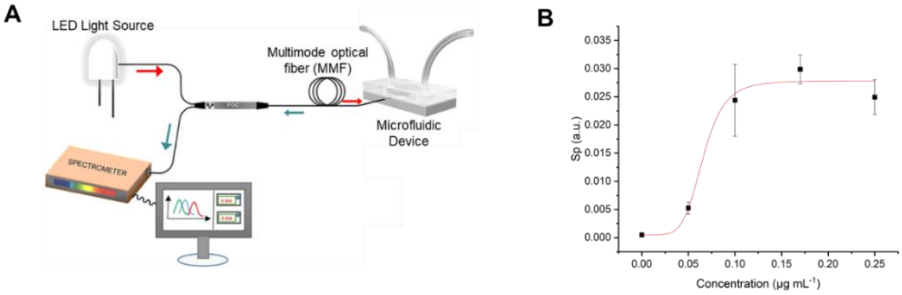


*Fig 1*. A) Squematic representation of the optical set-up with the integration of the microfluidic device. B) Graphical representation of VEGF quantification after 2 min of AuNP revealed ($R^2$=0.994).

**Acknowledgments**

This work was supported by the financial support of the Basque Government under the consolidated groups with grant no IT 1633 22 and the project PDC 2023 145917 I 00 funded by MICIU/AEI 10 13039 501100011033 and by the European Union Next GenerationEU /PRTR. The project is also supported by the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska Curie grant agreement No 101034379.

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# Evaluation of PCSK6 expression and secretion in Testicular Germ Cell Tumors by immunohistochemistry and CellStudio platform

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**Abstract**

Testicular germ cell tumors (TGCTs) are the most common solid malignancy in young men, comprising seminomas, which are generally less aggressive, and non-seminomas, which are highly invasive and prone to metastasis. Reliable molecular markers to predict tumor aggressiveness are still lacking. Here, we investigated proprotein convertase subtilisin/kexin type 6 (PCSK6), previously implicated in invasion and metastasis in other tumor types, as a potential biomarker of TGCT aggressiveness. Immunohistochemical analysis of patient-derived tissues revealed distinct expression patterns: in healthy testis, PCSK6 was restricted to post-meiotic cells; in seminomas, it was broadly distributed; and in non-seminomas, expression was confined to epithelial-like cells (Figure 1). To study TGCT subtypes in vitro, we used the seminoma-derived TCam-2 and the non-seminoma-derived NTERA-2 cell lines and the CellStudio platform, which allows to detect cell secretion from small cell clusters with high spatial resolution. The more aggressive NTERA-2 cells exhibited stronger staining and secreted higher levels of PCSK6 than the less aggressive TCam-2 cells, indicating a correlation between PCSK6 and tumor aggressiveness. These findings suggest that PCSK6 expression and secretion are tumor-type-specific and linked to aggressiveness, highlighting its potential as a biomarker for rapid stratification of TGCTs and early identification of aggressive tumors to guide personalized therapy.

**Keywords:** testicular germ cell tumors, PCSK6, tumor aggressiveness, metastasis

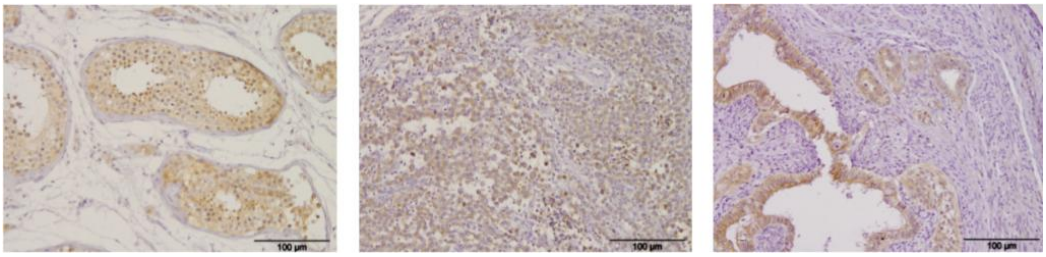

Figure 1. PCSK6 immunohistochemical staining (brown) in testicular tissue. Left: healthy testis showing strong expression in germinal epithelium of seminiferous tubules. Middle: seminoma with broader but weaker distribution. Right: non-seminoma with high expression restricted to epithelial-like cells.

**Acknowledgments**

We thank Dr. Ana Loizaga Iriarte (Hospital de Cruces, Osakidetza) for her assistance in handling cancerous samples. We also acknowledge the financial support from the Basque Government (GIC21/158, IT1633-22) and the Ministerio de Ciencia e Innovación/AEI/FEDER (PID2024-155781NB-I00).

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# FLASH POSTER PRESENTATIONS

# Towards Reliable Preclinical Testing: Early-Stage Development of a Bioprinted 3D In Vitro Chronic Wound Model

Mikel Salmeron[1,2]*, Lander Ruiz[1], Koro de la Caba[4,5,6], Pedro Guerrero[4,5,6], Manoli Igartua[1,2,3], Rosa Maria Hernandez[1,2,3] and Edorta Santos-Vizcaino[1,2,3].

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**Abstract**

Chronic wounds are a growing clinical burden, yet current animal models and simple monolayer cultures poorly predict human responses to therapy [1,2]. We present a 3D bioprinted in vitro chronic wound model as a more reliable and biologically relevant platform for reproducible preclinical drug testing. The model features a depression that mimics the wound, enabling quantitative analyses of closure, and a transwell system that recapitulates human skin physiology by permitting an apical air–liquid interface and a basal supply of nutrients. The bioink, composed of a mixture of natural and synthetic polymers, offers excellent printability due to its rheological properties. It maintains the printed geometry for at least 15 days through a curing process free of harmful crosslinking agents. Cytocompatibility was confirmed by a LIVE/DEAD assay using L929 cells (Fig. 1). These findings position the bioink as a viable basis for an in vitro chronic wound model, laying the groundwork to incorporate physiologically relevant cells and recreate the inflammatory microenvironment characteristic of chronic wounds.

**Keywords:** 3D bioprinting, chronic wound model, transwell system, preclinical drug screening.

**Graphical abstract:**

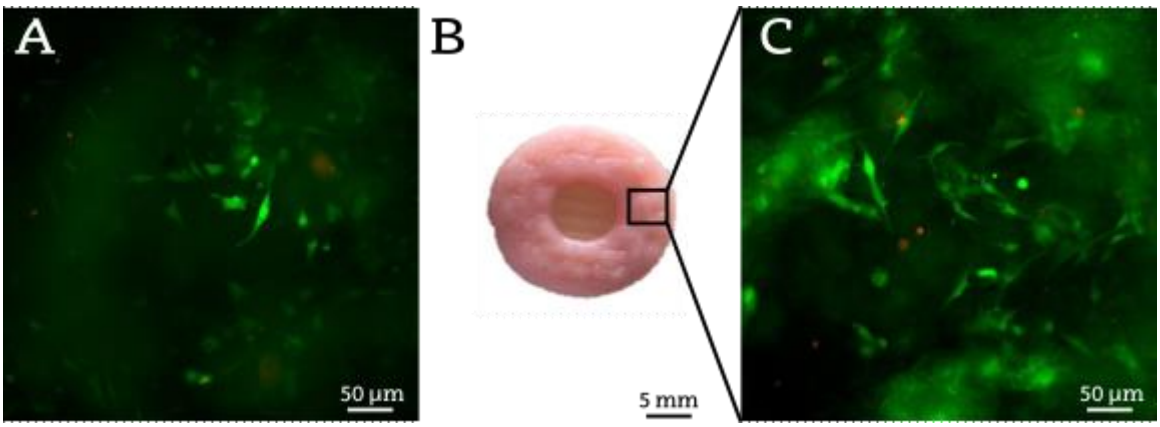


*Fig 1*. Live & dead assay of the bioink with L929 cells. A. Image of cells seeded on the bioink. B. Construct appearence. C. Image of cells inside de bioink.

**Acknowledgments**

This work was supported by the Basque Government (Bio3Dcron 2023111029, IT1448-22). Mikel Salmeron thanks the Basque Government for the PhD grant (PRE_2024_1_0230).

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# An *in vitro* model of human glioblastoma multiforme to study early-stage glioma progression in the tumour-associated microenvironment

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**Abstract**
Glioblastomas (GBMs) are a high-grade subset of gliomas. With their severe malignancy and resistance to standard-of-care therapies, they are among the most fatal refractory solid tumours. Studies on the key mechanisms underlying the dynamic interplay between the tumour and its microenvironment established the urgent need for reliable *in vitro* models to facilitate the investigation of cancer niche development and initial phases of tumour progression [1,2]. A novel model of GBM, constituted by a cancerous core of glioblastoma cells (U87-MG) surrounded by a hosting neuronal-like tissue shell (SH-SY5Y), is here proposed. The foremost aim is to set a preliminary systematic representation of a cancer niche and analyse the proliferation ability and invasiveness of the core tumoral mass. To this end, the development of the central GBM mass has been closely followed in relation to the neuronal-like adjacent cellular microenvironment. To increase tumour microenvironment representativeness and lay the ground for a more robust investigation at the cancer niche level [3], SH-SY5Y neuroblastoma cells have been guided to differentiate into neuron-like cells. This cellular model will serve as the framework for future 3D-bioprinted GBM models, in which the extracellular matrix (ECM) biomechanical impact can also be modulated.

**Keywords:** Glioblastoma, Cancer niche, Tumour progression, Neuronal differentiation

**Graphical abstract:**

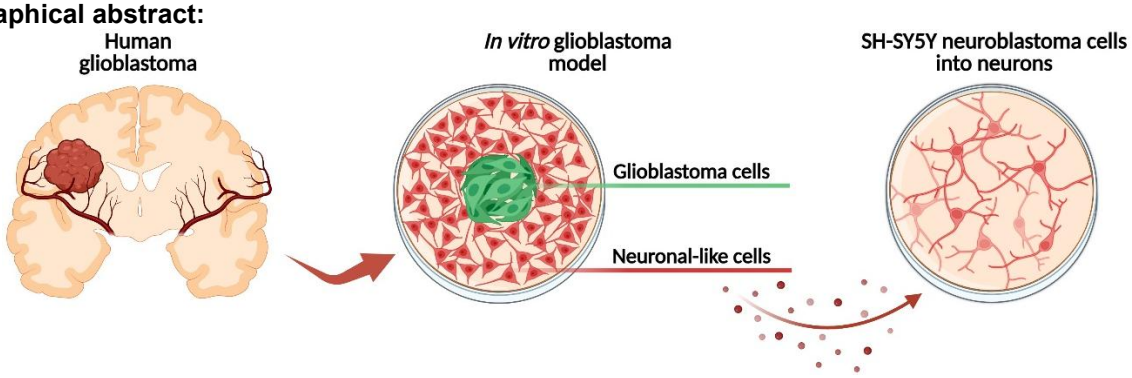


***Fig 1.*** *In vitro* exemplification of a human glioblastoma. A cancerous core of glioblastoma cells is here surrounded by a neuronal-like cell line. The neuroblastoma cells are then differentiated into neurons, in the aim of more closely representing the tissue that typically encloses the tumoral mass.

**Acknowledgments**
This work is supported by the DTRIP4H project, funded by Horizon Europe EU's funding program (No. 101188432).

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# NUTRITIONAL INTERVENTIONS IN CELIAC DISEASE: TOWARDS A HOLISTIC MANAGEMENT AND FUTURE CHALLENGES

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**Abstract**

Celiac disease (CD) is a chronic immune-mediated disorder that is triggered by the ingestion of gluten in genetically predisposed individuals [1]. Although a gluten-free diet (GFD) is the only effective treatment, it is often nutritionally imbalanced [2], and patients rarely receive adequate dietary support [3]. This can compromise the quality of the diet and have a negative impact on long-term health [4].

This thesis had two main objectives: (i) identifying the key perspectives required for comprehensive CD follow-up, and (ii) evaluating the impact of continuous face-to-face dietary interventions on pediatric patients. A narrative review revealed that optimal CD management must consider four areas: clinical, nutritional, psychological and social [5]. Two multicentre studies were conducted: the first (2016–2018, n = 58) included children and adults, implementing dietary intervention with periodic follow-up, while the second (2020–2023, n = 46) focused on children, including ongoing and face-to-face support.

In the first study, limited improvements were observed in dietary balance and symptoms. In contrast, the second study showed that continuous follow-up improved dietary habits, promoted greater adherence to the Mediterranean diet and supported the resolution of symptoms. However, quality of life scores remained low, highlighting the need for additional strategies.

The *GlutenFreeDiet* software, which was developed during this project, proved useful for monitoring diet quality and facilitating communication between professionals and patients [6]. A personalised dietitian-guided dietary assessment and continuous and face-to-face monitoring are beneficial in improving the nutritional status, dietary habits and symptoms of people with CD [7], but follow-up is not sufficient to improve quality of life. Future research should focus on developing more comprehensive digital tools that integrate nutritional education, follow-up and messaging functions, exploring psychological interventions for pediatric patients and validating non-invasive biomarkers to monitor GFD adherence (Figure 1).

**Keywords:** celiac disease, gluten-free diet, nutrition intervention, follow-up

**Graphical abstract:**

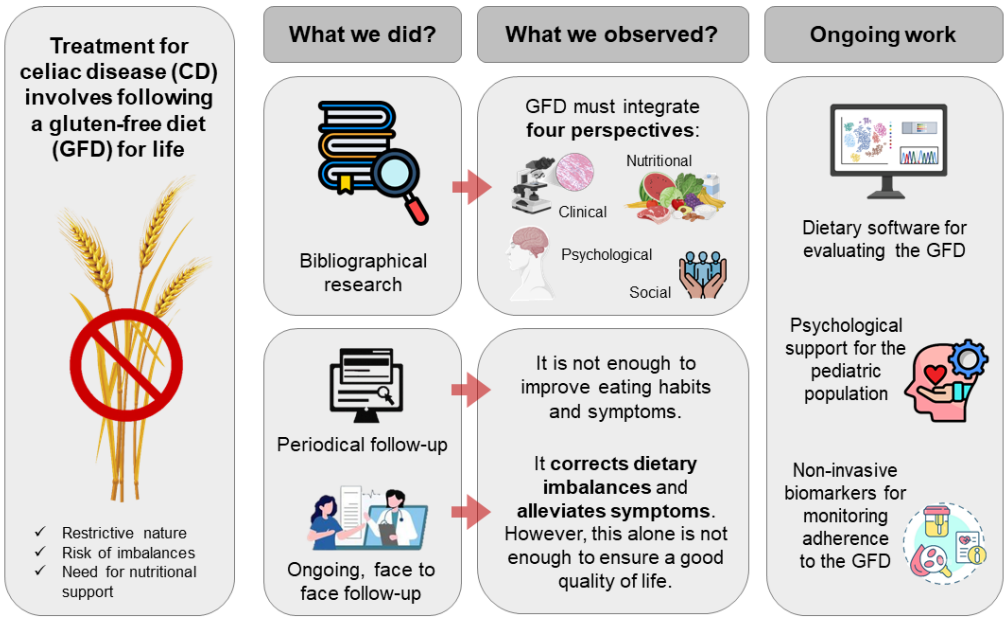


*Figure 1*. Graphical summary of the doctoral thesis: from nutritional monitoring in CD to future research perspectives.

## Acknowledgments

This work was supported by four grants from the University of the Basque Country (UPV/EHU): University–Society projects US15/06, US18/15, US20/16, and US22/22. The GLUTEN3S research group is also supported by a grant from the University of the Basque Country (GIU 18/78) and is recognized by the Basque Government (IT-1419-19). In addition, this work was funded by the Spanish Ministry of Science and Innovation (MCIN/AEI/10.13039/501100011033), through the I+D+i project PID2021-125695OA-I00, and co-funded by the European Regional Development Fund (ERDF, “A way of making Europe”).

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# Identification of novel genes potentially involved in the biofilm-forming ability of *Arcobacter butzleri*

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**Abstract**

Biofilm formation is a major virulence factor in many bacteria, including the zoonotic foodborne pathogen *Arcobacter butzleri*. Understanding the genetic mechanisms underlying biofilm development and maintenance is essential for designing effective control strategies to limit their dissemination and associated clinical manifestations, such as enteritis, endocarditis, peritonitis, and bacteraemia.
In this context, transposon-mediated random mutagenesis constitutes a valuable methodological approach. It enables genomic analysis in situations where alternative genetic manipulation techniques are unavailable [1], as is the case of *A. butzleri.* The EZ-Tn5 <KAN-2> transposome and *A. butzleri* strains RM4018$^T$ and P8 where use for this purpose. A total of 29 genes were identified as potentially involved in biofilm formation; including, *fdhA, fdhB1, fliD, fliH, glyA, lutB, metH, oprF, pdxH, typA,* and *ccoG*. Mutations in these genes led to a significantly reduced adherent phenotype, as assessed by the crystal violet assay on 96-well polystyrene plates. Moreover, several mutants also exhibited alterations in other traits, including motility, antimicrobial resistance profiles, lactate metabolism, cold sensibility and methionine auxotrophy.
This study therefore not only highlights the potential of transposon mutagenesis as a tool for genetic analysis in arcobacters, but also expands current knowledge by identifying new genetic determinants implicated in *A. butzleri* biofilm formation. This constitutes the primary phase in the functional genetic characterisation of novel genes in this under-researched bacterial species.

**Keywords:** *Arcobacter butzleri*, Transposon mutagenesis, Biofilm.

**Graphical abstract:**

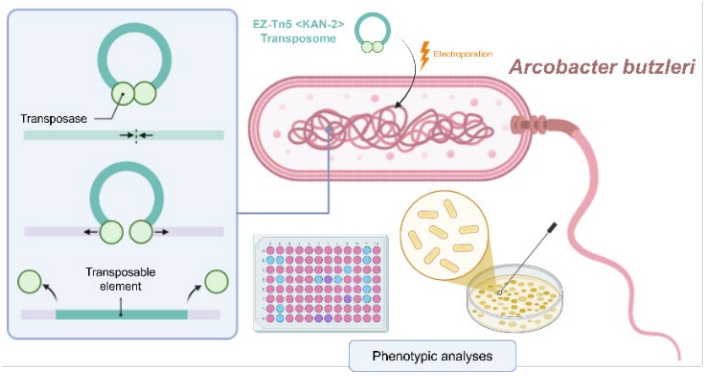


*Fig 1*. Summary methodology performed for the transposon mutagenesis of *A. butzleri*.

**Acknowledgments**

This work was supported by the University of the Basque Country UPV/EHU, grant number PPG17/27, and by the Basque Government, grant number PA20/03. A.S.-S. received a Ph.D. fellowship from the University of the Basque Country UPV/EHU.

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# Analytical techniques for identifying anthropogenic fire in Middle Pleistocene sediment samples

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**Abstract**

The control of fire by human groups represents an adaptive strategy that profoundly transformed prehistoric lifeways; however, its dynamics remain poorly understood. This study aims to identify and characterize the anthropogenic or natural origin of fire evidence at two Iberian archaeological sites dated to 400–300 ka: Sima del Elefante (Atapuerca, Spain) and La Cansaladeta (La Riba, Spain). Polycyclic aromatic hydrocarbons (PAHs) were analyzed using GC-MS. PAHs are organic compounds generated during the partial combustion of organic matter: light PAHs (3–4 rings) are typically linked to wildfire emissions, while heavy PAHs (5–6 rings) are associated with wood burning [1]. However, the selectivity of these compounds is not enough to confirm undoubtedly the origin of the fire, therefore, methodologies from health and environmental sciences were adopted, specifically the search for persistent and specific archaeological biomarkers through Omics approaches using liquid chromatography coupled with high-resolution mass spectrometry to predict the origin of the fire [2]. Combustion residues contain an organic fraction with strong potential for lipid content; thus, lipidomic is proposed as a promising avenue [3]. Consequently, an innovative strategy is proposed, grounded in experimental archaeology (generation of contemporary samples) to idenfy selective archaeological biomarkers for fire identification and subsequently applied to archaeological specimens.

**Keywords:** Fire, archaeological-biomarkers, GC-MS, lipidomic.

**Graphical abstract:**

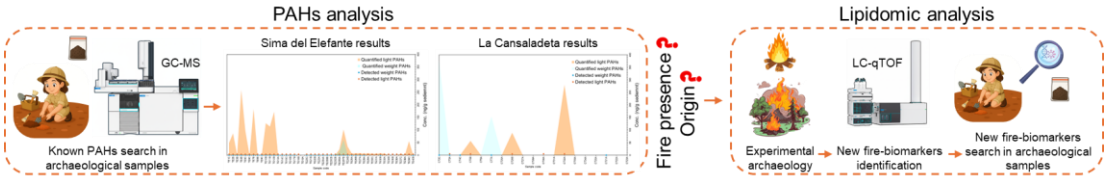


*Fig 1*. Schematic representation of the research workflow

**Acknowledgments**

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# Bioactive hydrogel coatings on titanium implant surface simulators

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**Abstract**

Titanium-based implants are widely used in orthopedic and dental applications due to their excellent mechanical properties, corrosion resistance, and non-magnetic behavior. However, they present certain limitations in terms of biocompatibility, which may compromise their integration with the biological environment. [1] In recent years, hydrogel coatings have emerged as a promising strategy to enhance the biocompatibility, biodegradability, and bioactivity of these implants. Most of these coatings can promote cell adhesion, proliferation, and differentiation, while also providing antibacterial and immunomodulatory properties.[2]

The most common methods for applying these coatings include spin coating, dip coating, spray coating, electrodeposition, and photopolymerization.[3] In this work, hidrogel coatings were developed on titanium substrates (Ti6Al4V) using formulations of hyaluronic acid (HA) and hydrolyzed collagen (COL) crosslinked with 1,4-butanediol diglycidyl ether (BDDE), as well as formulations of chitosan (CHI) and collagen crosslinked with genipin (GP). To achieve stable chemical bonding with the metallic surface, self-assembled monolayers (SAMs) were employed as a surface functionalization method.

The CHI-COL coatings exhibited significant antimicrobial activity, while the HA-COL systems enabled sustained drug release, reaching up to 75% release under controlled conditions. These results highlight the potential of functionalized hydrogels as active coatings to improve the clinical performance of titanium implants in biomedical applications.

**Keywords:** bioactive, hydrogel, coatings, titanium

**Graphical abstract:**

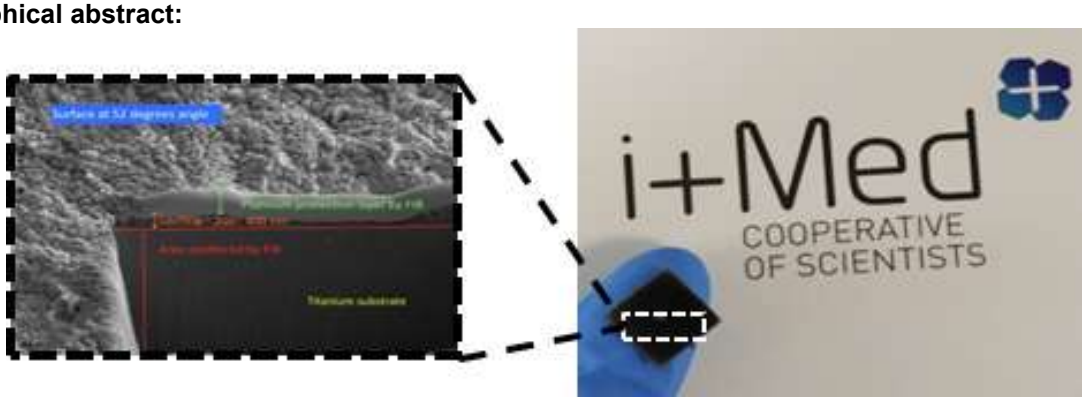


*Fig 1*. CHI-COL hydrogel coatings on titanium surface

**Acknowledgments**

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# Development and characterization of heparin-loaded bioinks for 3D bioprinting of elastic tissue

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**Abstract**

The regeneration of elastic tissues, such as tendons, using 3D bioprinting requires bioinks with suitable physical, chemical and biological properties [1], [2]. In this study, an ink based on the biomaterials alginate, fibrillar nanocellulose, carboxymethyl chitosan and hyaluronic acid aldehyde was developed and characterized. In addition, heparin was incorporated at different concentrations (0%, 1% and 3% w/v) to evaluate its effect on structure and controlled release for possible biomedical applications. For the characterization of the bioink, the following parameters were evaluated: pH, rheological behavior, printability, textural properties, swelling, degradation, morphology, heparin release profile, and cell viability. All formulations showed shear-thinning behaviour that allowed extrusion printing and rapid recovery. The texture study showed adequate mechanical properties in all formulations. The highest swelling ratio was observed in the ink without heparin, followed by the ink containing 1% and 3% heparin, and the percentage of degradation in all cases remained above 80% after 8 days. The heparin release profile followed the same trend for both inks, reaching 70% and 60%, respectively. Preliminary cell viability tests showed suitable biocompatibility in all three inks. In summary, the incorporation of heparin does not influence the rheological or functional properties and offers controlled drug release. These formulations are a promising strategy for the manufacture of elastic tissue constructs and their future use in regenerative medicine.

**Keywords:** biomaterials, heparin, 3D-bioprinting, ink development

**Graphical abstract:**

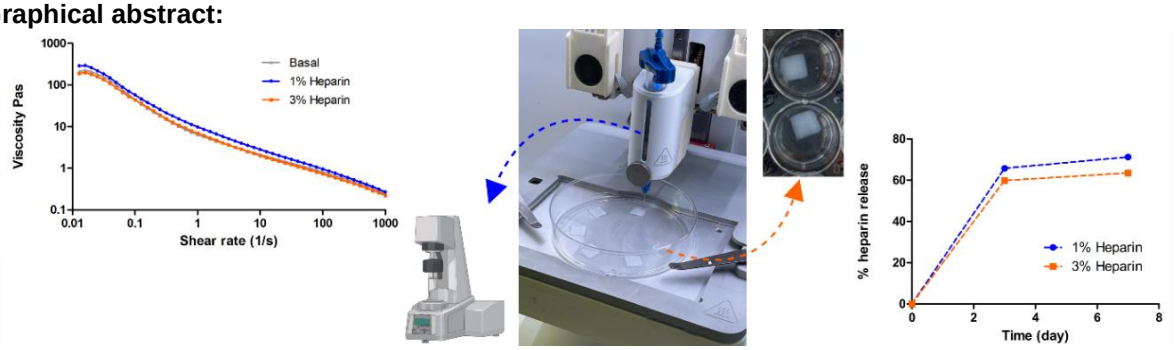


*Fig 1*. Rheology results and heparin release profile on ink and 3D-printed scaffold, respectively.

**Acknowledgments**

This work is part of the R&D&I CPP2021-008754 project, funded by MCIN/ AEI/10.13039/501100011033/ and by the 'European Union NextGenerationEU/PRTR'. This research was also supported by CIBER (CB06/01/1028, ISCIII, Ministry of Science and Innovation) and by the Basque Country Government (Consolidated Groups, IT1448-22).Authors wish to thank the intellectual and technical assistance from ICTS Nanbiosis (U10, CIBER-BBN) at UPV/EHU.

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# Pharmacological inhibition of mTOR improves hERG channel performance in a cellular model of LQTS2

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**Abstract**

Congenital Long QT Syndrome (LQTS) is an inherited cardiac disorder characterized by an excessive prolongation of the Q-T interval. This condition leads to an increased susceptibility to arrhythmias and sudden cardiac death [1]. Approximately 40% of congenital LQTS cases are classified as type 2 (LQT2), which are caused by mutations in the KCNH2 gene. This gene encodes the cardiac potassium channel Kv11.1, also known as hERG, which mediates the rapid delayed rectifier potassium current (IKr) [2]. Current treatments are ineffective in 30% of patients, making it necessary to explore new therapeutic alternatives [3].
Our research group has demonstrated an increase in the functional expression of the hERG ion channel following treatment with a drug from the Rapalog family that inhibits mTOR (Rapa). We are currently investigating the potential repositioning of this drug as part of the therapeutic arsenal for LQT2.
The current objective is to determine whether Rapa enhances the functionality of mutated hERG channels (E58G, Y427C, R531W, and L1012Pfs*55) responsible for LQT2 syndrome, which could represent a potential new therapeutic target for treating this condition.

Patch clamp results show that Rapa increases the functionality of all four mutated hERG channels. For the E58G, Y427C, and L1012Pfs*55 mutations, this increase does not restore current density to wild-type (WT) levels. However, in the case of the R531W mutation, current density exceeds that of the WT channel.

**Keywords:** Congenital Long QT Syndrome type 2 (LQT2), Rapalogs, Mutated hERG Channels.

**Graphical abstract:**

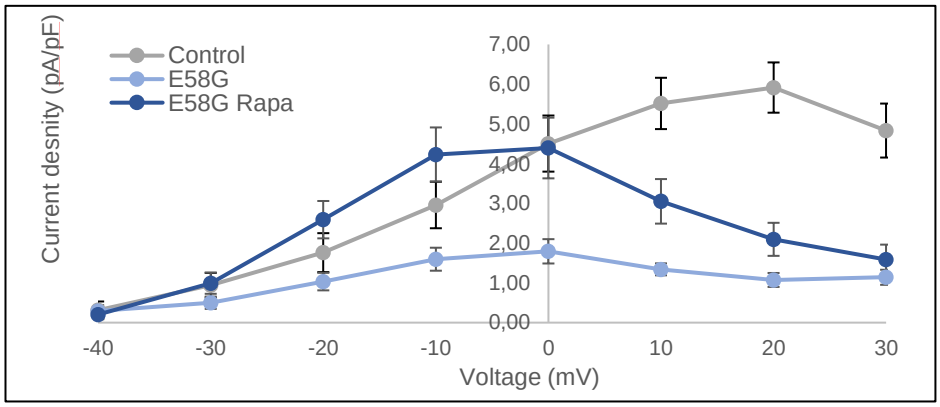


*Fig 1*. hERG current density at different voltages in HEK-HERG cells transfected with DYK-KCNH2 (control) and DYK-E58G, without incubation (E58G) and incubated with 5 μM Rapa for 24 h (E58G Rapa).

**Acknowledgments**
This research was supported by the Government of the Autonomous Community of the Basque Country (IT1707-22) and the Spanish Ministry of Science and Innovation (PID2020-118814RB-I00). B.S-D received support from a UPV/EHU predoctoral (PIF 21/313) contract.

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# 3D bioprinted vascular constructs with ECM-mimetic properties: Functional and structural analysis

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**Abstract**

Vascular bypass grafting is the primary strategy to restore blood flow in patients with vascular occlusions. Although autologous grafts are preferred, their availability is often limited, especially in patients with comorbidities [1]. This study presents a biomimetic, multilayer vascular construct fabricated via extrusion-based 3D bioprinting, using a novel ECM-mimicking bioink made of natural components only and embedded with human cells, without synthetic reinforcement.

A three-layered tubular structure was printed, incorporating (from lumen outward) HUVECs, hSMCs, and hFIBs [2], each in tailored bioinks.

Cell viability assays and live imaging confirmed high survival and proliferation. Fluorescent imaging with GFP/RFP-labelled cells showed proper spatial organization and dynamic behavior.

This study offers a promising approach for future developments in regenerative medicine and disease modeling.

**Keywords:** 3D bioprinting, vascular tissue engineering, ECM-mimicking bioink, cell viability.

**Graphical abstract:**

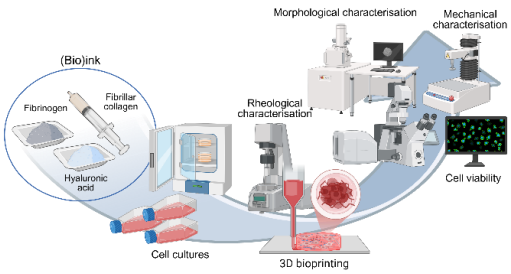


*Fig 1*.outline of the methods used to characterisethe bioink.

**Acknowledgments**

This project was funded by the University of the Basque Country (UPV/EHU) and the Basque Government (Grupos Consolidados, ref: IT1448-22). We thank ICTS “NANBIOSIS,” especially the Drug Formulation Unit (U10) of CIBER-BBN at UPV/EHU, for technical support. DS acknowledges EU funding through the H2020-MSCA-COFUND-2020-101034228-WOLFRAM2 project.

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# SYNTHESIS OF NITROGEN HETEROCYLES AS HUMAN TOPOISOMERASE I INHIBITORS

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**Abstract**

Over the years, a great effort has been made to discover and develop new anticancer drugs. Among the drugs used in chemotherapy we can find the called topoisomerase inhibitors, which, currently are used in therapies that have topoisomerase I (Top I) and II (Top II) as their pharmacological target. In fact, the effectiveness of this type of inhibitors lies in the overexpression of Top I in cancer cells. Among the natural anticancer drugs targeting Top I, the most representative example is camptothecin (CPT) [1], however, the antitumor activity of CPT decreases rapidly at physiological conditions (pH: 7.4, 37ºC) [2].

In this work, a new methodology is reported for preparation of chromeno[4,3-d]pyrido[1,2-a]pyrimidines by an intramolecular Povarov reaction using appropriate substrates such as 2-pyridylamine, suitably functionalized aldehydes and under activation by Brønsted acids (***Fig 1***) [3]. In addition, the biological activity of the new heterocycles was tested, and as a result, some of them showed good inhibition against human Top I enzyme and high cytotoxicity against different cancerous cell lines.

**Keywords:** cancer, topoisomerase I inhibitors, heterocycles, camptothecin.

**Graphical abstract:**

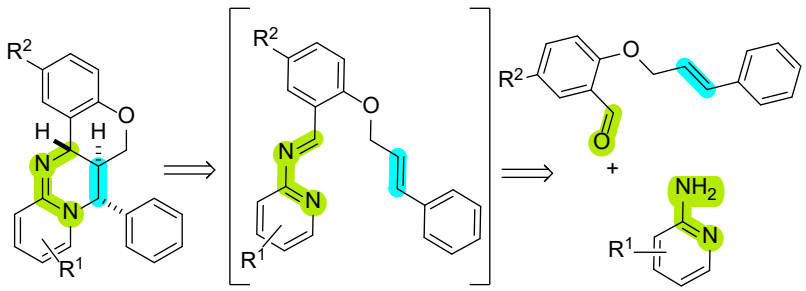


*Fig 1*. Retrosynthesis of new polyheterocyclic derivatives

**Acknowledgments**

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# Single-Cell Adhesion Dot Array (SCADA) enables high-resolution profiling of breast cancer cell–matrix interactions

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**Abstract**
Tumour–microenvironment interactions strongly influence cancer progression, invasion and metastasis [1]. Cell adhesion to extracellular matrix (ECM) proteins reflects both biophysical traits and malignant behaviour [2]. Here, we applied the Single Cell Adhesion Dot Array (SCADA) [3], a microarray-based biosensor, to quantify adhesion of two breast cancer cell lines to fibronectin, collagen I and collagen IV. Two phenotypic cells types were compared: triple-negative breast cancer (TNBC; MDA-MB-157), known for its high invasiveness, and non-TNBC (BT474), which display more epithelial features. Cells were seeded on UV-patterned SCADA substrates, enabling precise confinement and digital scoring of adhesion events with minimal reagents. TNBC cell line showed consistently lower adhesion to all ECM components than non-TNBC line. This reduced affinity suggests an association between weak ECM attachment and mesenchymal or migratory phenotypes. Conversely, stronger adhesion by non-TNBC cells correlates with their more differentiated, less invasive behaviour. These findings demonstrate SCADA's utility for high-resolution profiling of cell–ECM interactions. By linking adhesion patterns to tumour phenotype, this approach may provide a practical tool for stratifying cancer aggressiveness and may inform the development of adhesion-based biomarkers for drug testing and personalised oncology.

**Keywords:** cell adhesion, affinity, Breast cancer, microfluidics.

**Graphical abstract:**

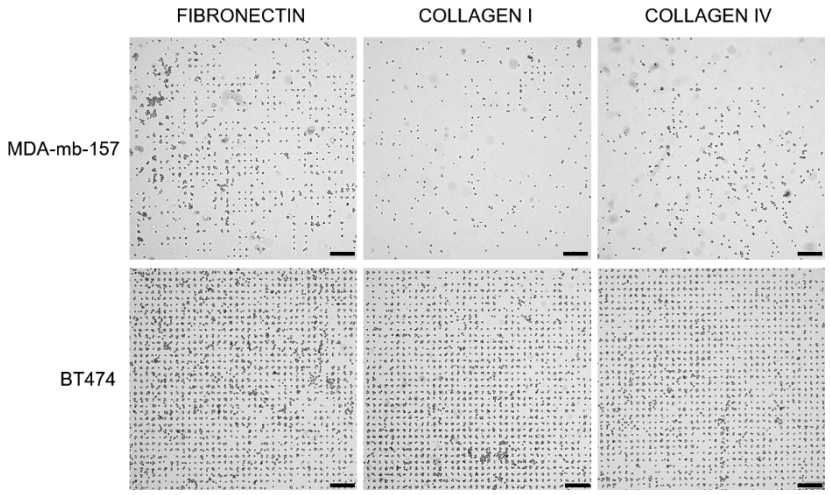


*Fig 1*. Comparison of 2 different subtypes of Breast cancer towards Fibronectin, Collagen I and Collagen IV. Scale bar mean: 200 µm

**Acknowledgments**
This work was supported by Research project MICROFLUIDICS & BIOMICS Cluster UPV/EHU (IT1633-22) financed by Basque Government and by the Ministerio de Ciencia, Innovación y Universidades, the Agencia Estatal de Investigación (AEI, 10.13039/501100011033), and the European Regional Development Fund (FEDER, EU), under project PID2024-155781NB-I00.

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# A paper-based microfluidic device for the colorimetric detection of scopolamine with the naked eye

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**Abstract**

This study focuses on the development of a microfluidic paper-based device for the rapid detection of scopolamine, a drug increasingly associated with drug-facilitated sexual assaults (DFSA) [1]. Microfluidic paper-based analytical devices (μPADs) offer simple, low-cost platforms capable of analyzing diverse matrices on-site [2][3]. Detection in this device is based on Scott's reaction on a solid support, where scopolamine forms a colored complex with cobalt(II) thiocyanate in an acidic medium, producing a visible pink to blue shift. The multi-layered design combines cellulose paper and polymeric materials, achieving a visual detection limit between 0.5 mg $mL^{-1}$ and 1.0 mg $mL^{-1}$. This autonomous and portable platform provides a practical tool to enhance forensic investigations and preventive strategies against DFSA.

**Keywords:** scopolamine, microfluidic device, colorimetric reaction, matrices.

**Graphical abstract:**

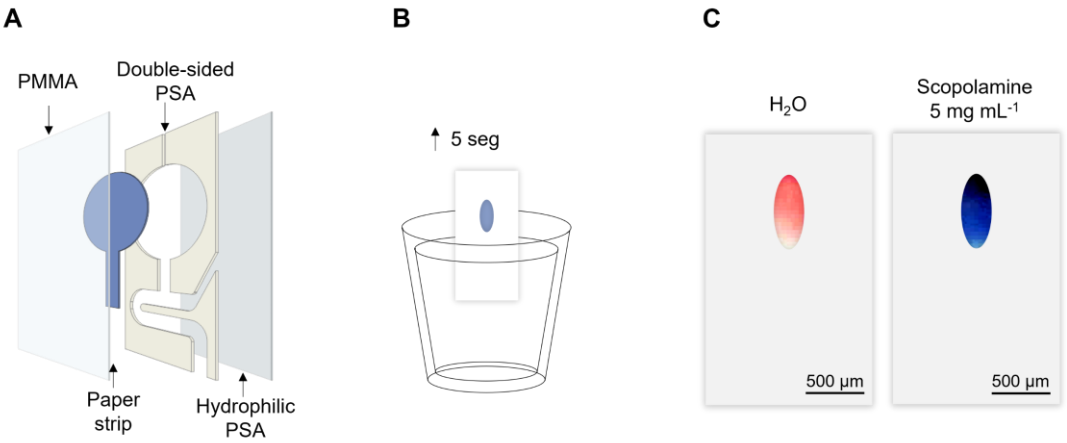


*Fig 1.* A) Scheme of the different layers forming the scopolamine microfluidic device test. B) Scheme of the protocol followed for analysis. C) Images of the scopolamine microfluidic device, showing a negative result and a positive result in scopolamine.

**Acknowledgments**

This work was supported by Research project MICROFLUIDICS & BIOMICS Cluster UPV/EHU (IT1633-22) financed by Basque Government, the Ministerio de Ciencia, Innovación y Universidades, the Agencia Estatal de Investigación (AEI, 10.13039/501100011033), and the European Regional Development Fund (FEDER, EU), under project PID2024-155781NB-I00. We acknowledge funding support from the University of the Basque Country and the Spanish Government under the 35 program "Margarita Salas" funded by "Unión Europea-Next Generation EU". Isabel Poves-Ruiz acknowledges the Basque Government for the Predoctoral grant "PRE_2023_1_0061". We acknowledge Professor Igor Horrillo Furundarena of the Neuropsychopharmacology Group of the University of the Basque Country (UPV/EHU) for providing the *Atropa Belladonna* and *Datura Stramonium*.

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# SLAMF3 Expression and Adhesion Dynamics of Jurkat Cells in Microfluidic Device

A. G. Casado-Cedano[1,2]*, N. Lartitegui-Meneses[1], F. N. Nazar[1], P. E. Guevara-Pantoja[1], F. Benito-Lopez[1], I. Postigo[1,2] and L. Basabe-Desmonts[1,3]

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## Abstract

Microfluidic systems offer unique opportunities to study immune cell behavior under controlled and physiologically relevant conditions. Within this context, SLAMF3 (CD299) emerges as a biomarker critically involved in T cell activation and differentiation, whose dysregulated expression has been linked to autoimmune diseases and metabolic disorders [1].
In this abstract, Jurkat T cells were cultured and transferred into a microfluidics device (*CellStudio*) patterned with fibronectin (100µg $mL^{-1}$) to evaluate the dynamics of adhesion and biomarker expression [2]. Cells were either left unstimulated or stimulated in situ with anti-CD3, anti-CD28, and a pro-inflammatory cytokine cocktail (IL-6, IL-1β, IL-23, IL-21 and TGF-β1) [3]. The result revealed that stimulated cells adhered less efficiently to fibronectin patterns compared to unstimulated ones, but displayed significantly higher SLAMF3 expression. These findings indicate that the stimulation influences cell phenotype and alters adhesion, demonstrating the suitability of the microfluidic device to monitor biomarkers in T cell. Compared to other methods, this approach provides the advantage of simultaneously analyzing adhesion and receptor expression in a spatially organized microenvironment, opening avenues for precision immunology studies.

**Keywords:** Microfluidics; T cells; SLAMF3; Adhesion.

## Graphical abstract:

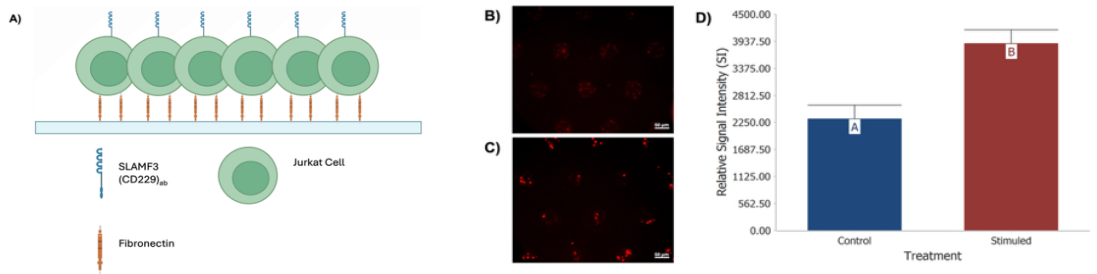


***Fig. 1. Stimulation study of Jurkat cells in CellStudio.*** *A) Graphical scheme of Cellstudio platform showing Jurkat cell islets. B-C) Representative fluorescence images acquired with the CellStudio platform, showing signal intensity in unstimulated (B) and stimulated (C) cells. D) Quantification of relative mean fluorescence intensity (SI) obtained from image analysis, different leters (A, B). are indicative of statistically significant differences (P < 0.05).*

**Acknowledgments** This work was funded by the Ministerio de Ciencia, Innovación y Universidades, Agencia Estatal de investigación (AEI, 10.13039/501100011033), and the European Regional Development Fund (FEDER, EU) under project PID2024-15578NB-100. We also thank funding support from Basque Government, under Grupos Consolidados with Grant No. IT1633-22.

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# Development of dECM-Based Bioinks for 3D Bioprinting of Tendon Tissue

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**Abstract**

Tendon injuries remain a major clinical challenge, with current therapies often failing to achieve complete functional regeneration [1]. Tissue engineering offers promising alternatives, but designing bioinks that combine printability with biological relevance is still difficult. That is why novel bioactive materials like decellularized extracellular matrix (dECM) are of particular interest since they retain the biochemical and structural cues of native tissues, fostering cell viability and tenogenic differentiation [2]. However, before dECM can be used to enrich bioinks, robust decellularization protocols must be established to remove cellular content while preserving key matrix components [3].

In this work, we focused on setting up and optimizing a tendon decellularization process, evaluating chemical, enzymatic, and physical strategies to achieve effective cell removal and retention of collagen and glycosaminoglycans. In parallel, printable hydrogel formulations based on gelatin, alginate, hyaluronic acid, and microfibrillated cellulose were developed and tuned for extrusion-based 3D bioprinting, showing suitable rheology, controlled degradation, and good cell compatibility. This study provides the basis for integrating tendon-derived dECM into bioinks, aiming to create highly bioactive materials for functional tendon regeneration.

**Keywords:** Hydrogel scaffolds, tissue engineering, decellularized extracellular matrices

**Graphical abstract:**

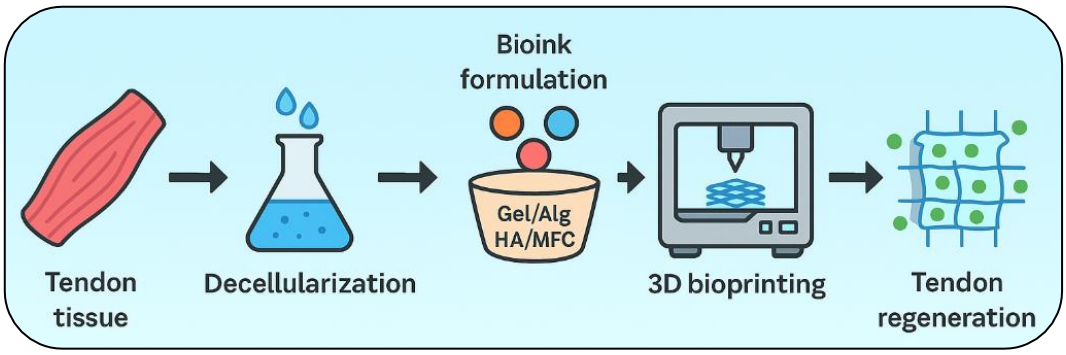


*Fig 1*. Workflow for the development of bioinks based on decellularized extracellular matrix (dECM) for tendon tissue engineering.

**Acknowledgments**

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## ORAL COMUNICATIONS
## Session II

# Effect of viable and inactivated *Lactobacillus rhamnosus* GG administration on the prevention of diet-induced obesity in rats: Implication of white and brown adipose tissue and influence of bacterial viability

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**Abstract**

Obesity, defined as an abnormal or excessive fat accumulation, is one of the most prevalent chronic metabolic alterations worldwide being highly related to an increased risk for further associated co-morbidities [1]. Current evidence indicates that subjects with obesity have a distinct gut microbiota signature, emphasizing gut microbiota composition as a potential factor determining its onset and progression [2]. The aim of this research is to evaluate the potential effects of viable and heat-inactivated *Lactobacillus rhamnosus* GG in the prevention of diet-induced obesity in a rat model. The administration of the probiotic or its heat-inactivated postbiotic prevented diet-induced WAT increase in a similar manner. While viable probiotic administration resulted in a reduced lipid uptake (LPL) and *de novo* lipogenesis (FAS), along with enhanced lipolysis (ATGL) in WAT, its heat-inactivated postbiotic mainly reduced *de novo* lipogenesis. Additionally, the obtained results demonstrated that probiotic administration enhanced thermogenesis (UCP1) and fatty acid oxidation (CPT-1b) on BAT, as well as upregulated several markers involved in mitochondrial biogenesis (p38 MAPK, NRF1 and CS). By contrast, despite the administration of the postbiotic upregulated thermogenesis and fatty acid oxidation in a comparable manner as the probiotic, these results were not accompanied by changes in mitochondrial biogenesis markers. These results indicate that under the specific experimental conditions tested, both the administration of viable and heat-inactivated *Lactobacillus rhamnosus* GG present valuable potential for preventing diet-induced WAT mass increase in rats. While both treatments exerted similar effects on WAT and BAT, subtle differences that may derive from bacterial viability were observed in the involved mechanisms of action.

**Keywords:** Obesity; Probiotics; Postbiotics; *Lactobacillus rhamnosus* GG.

**Graphical abstract:**

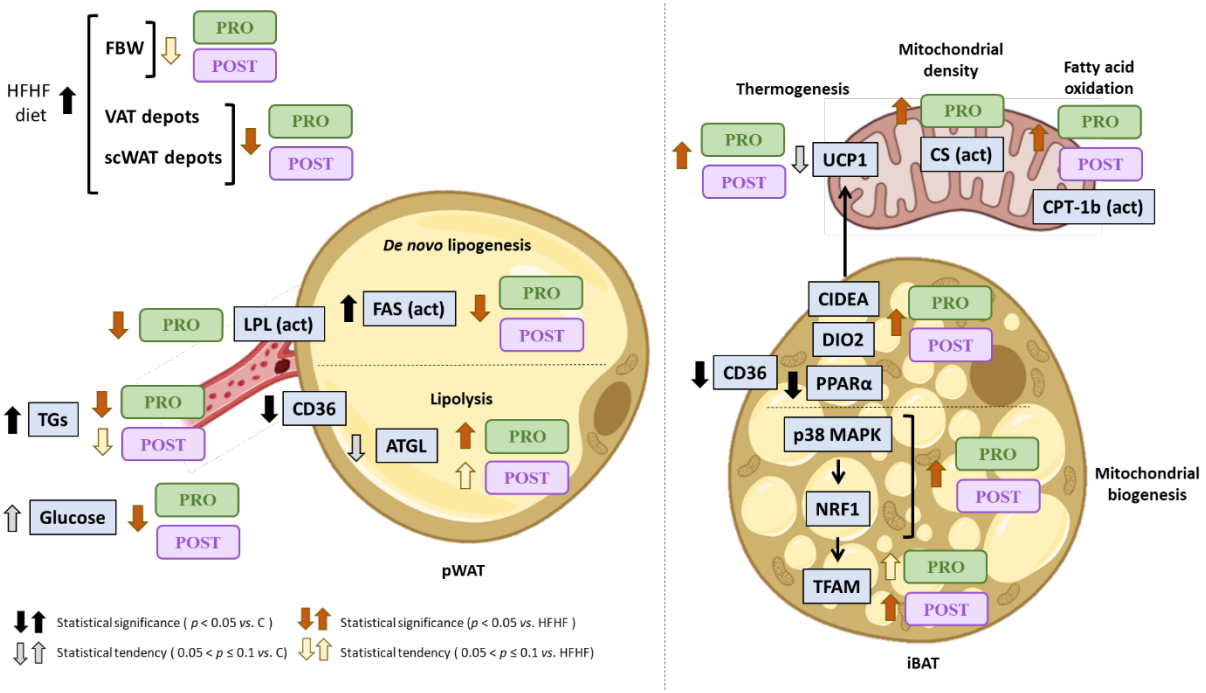


*Fig 1*. Graphical abstract showing the effects of viable and heat-inactivated L. rhamnosus GG in the white and brown adipose tissue of diet-induced obese rats.

## Acknowledgments

This study was supported by Instituto de Salud Carlos III (CIBERobn) under grant CB12/03/30 0 07 and the Basque Govern- ment under grant IT1482-22. Laura Isabel Arellano-García is a re- cipient of a doctoral fellowship from the Gobierno Vasco.

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# *E3 ligase Ube3a targets mTOR for degradation*

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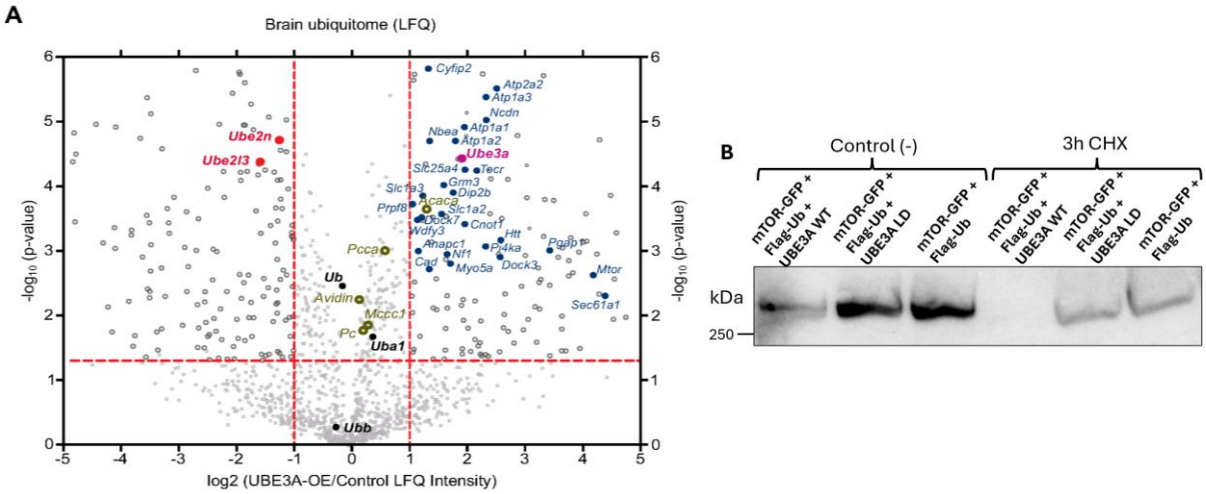
**Abstract**

Angelman Syndrome (AS) is a neurodevelopmental disorder caused by the lack of Ube3a in the brain, an E3 ligase involved in protein ubiquitination. In order to understand the molecular mechanisms underlying the disease, it is essential to know which are the substrates of Ube3a. However, to date, little is known about them. With the aim of identifying Ube3a substrates, we have performed a quantitative proteomics experiment to analyze the neuronal ubiquitome of mice overexpressing Ube3a [1]. We detected mTOR, a serine/threonine kinase involved in protein synthesis and synaptic plasticity [2], as a putative Ube3a substrate. Furthermore, we confirmed that human Ube3a ubiquitinates mTOR in the HEK293T cell line. Ubiquitin modifications control a plethora of essential cellular processes but was initially linked to protein degradation [3]. Due to this, we performed a cycloheximide degradation assay and established that Ube3a-dependent mTOR ubiquitination results in mTOR degradation. Thus, mTOR has been validated as a degradation target of Ube3a. Future experiments will focus on defining the exact residues of mTOR that Ube3a ubiquitinates, as well as discovering the deubiquitinases that counteract its activity.

**Keywords:** mTOR, ubiquitin, Ube3a, proteomics

**Graphical abstract:**




(A) Comparison of the abundance, determined by their LFQ intensities, of the ubiquitinated proteins identified by MS upon UBE3A overexpression relative to control mice. (B) WB showing the over time evolution of the degradative relationship between Ube3a and mTOR.

**Acknowledgments**

E.P.B. thanks the University of the Basque Country (EHU) for their research grant (PIF23/156). The work was supported by Dr. Kerman Aloria, Proteomics Core Facility Specialist at the Advanced Research Facilities (SGIker), UPV/EHU.

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# Novel antiplasmodial compounds *via* sulfadoxine modification through multicomponent reactions

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Artemisinin-based combination therapies (ACTs) are the first-line treatment for uncomplicated malaria and have been pivotal in global malaria control over the past decades. Among these, the combination of artemisinin with sulfadoxine and pyrimethamine (AS-SP) remains a key therapeutic option (Figure 1A). However, the increasing emergence of resistance to artemisinin and its partner compounds highlights the urgent need for the development of new and effective antimalarial agents.[1]

Drug repurposing and late-stage functionalization are powerful strategies for generating new pharmacologically active derivatives from existing drugs.[2] In line with this principle, alternative approaches, such as the use of multicomponent reactions (MCRs), have also been explored for the discovery of novel therapeutic agents.[3] In a previous work, this methodology was successfully applied to the derivatization of the known antibiotics sulfadoxine and dapsone, both of which feature an aniline moiety able of participating in Povarov and Ugi MCRs (Figure 1B). As a result, lipophilicity-enhanced derivatives were obtained, exhibiting remarkable activity against *Mycolata* bacteria.[4]

Herein, we broadened the scope of compounds previously developed from the WHO-listed essential medicine sulfadoxine by evaluating their antiplasmodial activity against the 3D7 wild-type *Plasmodium falciparum* strain, as well as strains resistant to chloroquine and atovaquone. Considering that sulfadoxine is currently co-administered with pyrimethamine and artesunate in approved ACT-based therapies, the antiplasmodial profiles of the new derivatives were assessed both individually and in combination with pyrimethamine to explore potential synergistic effects.

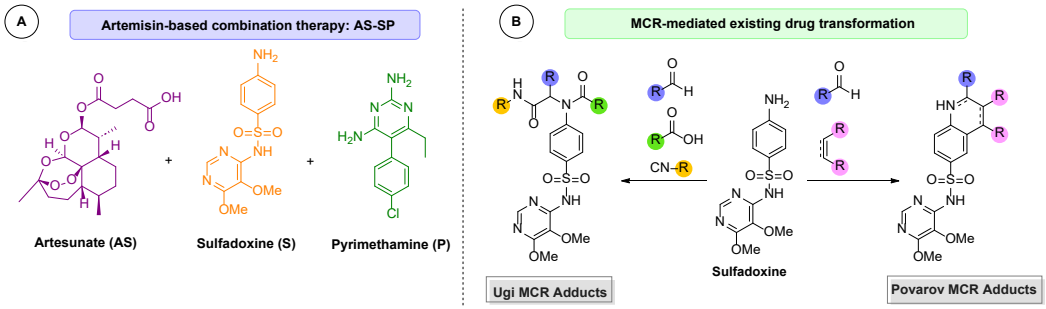


*Figure 1. (A) Chemical structures of the drugs comprising the artesunate-sulfadoxine-pyrimethamine (AS-SP) artemisinin-based combination therapy (ACT). (B) Synthetic routes employing Ugi and Povarov reactions on sulfadoxine to generate biologically active derivatives.*

**Acknowledgments**

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# Hybrid Metal–Organic Framework electrolytes for safer, high-energy rechargeable batteries

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**Abstract**

The rational design of advanced solid electrolytes is critical for the development of next-generation rechargeable batteries. Sodium-based rechargeable batteries are attracting increasing attention as a sustainable and cost-effective alternative to lithium systems. A key challenge in their development lies in designing solid electrolytes that combine high ionic conductivity, electrochemical stability, and mechanical robustness [1]. In this work, we combine Metal–Organic Frameworks (MOFs), acting as structural scaffolds and barriers against dendritic growth, with ionic liquids (ILs) confined within MOF nanopores to enable high ionic transport. Optimal loading of IL within the MOF pores results in a remarkable increase in ionic conductivity, achieving values up to $5 \cdot 10^{-4}$ S cm$^{-1}$ at room temperature, together with an acceptable $Na^+$ transference number. These solid electrolytes enable stable and dendrite-free Na plating/stripping over 100 h, while exhibiting an extended electrochemical stability window above 7 V *vs*. $Na^+$/Na. These findings demonstrate the potential of MOF–ionic liquid hybrid architectures as a rational strategy to advance the design of safe, high-performance solid electrolytes for next-generation sodium batteries [2].

**Keywords:** metal–organic framework; ionic liquid; solid-state electrolyte; sodium battery.

**Graphical abstract:**

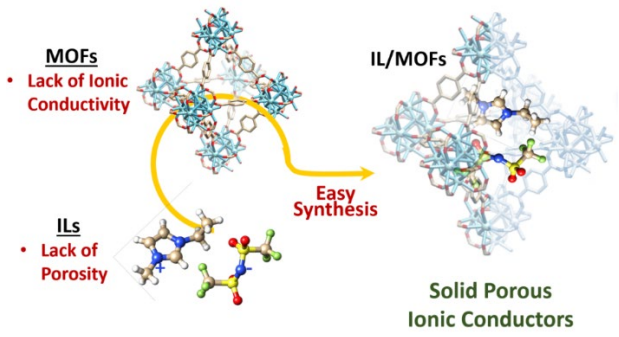


*Fig 1*. Design principle for next-generation solid electrolytes: integrating MOFs and ILs to achieve porous hybrid conductors with enhanced ionic conductivity.

**Acknowledgments**

This work was supported by MICIU/AEI/ 10.13039/501100011033 (PID2023-151153OB-I00, PID2021-122940OB-C31 and TED2021-130621B-C42) and by FEDER, UE. MCIN with funding from European Union NextGenerationEU (PRTR-C17.I1) and by the Gobierno Vasco under IT1546-22 project and the ELKARTEK and IKUR programs.

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## ORAL COMUNICATIONS
## Session III

# Prime-LS, a cryoprotectant-free lyophilized MSC-secretome providing complete protection against ulcerative colitis

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## Abstract

Ulcerative colitis (UC) is a chronic immune-mediated disorder of increasing prevalence worldwide, often unresponsive to conventional therapies and associated with high relapse rates and frequent colectomy. Cell-free approaches based on mesenchymal stromal cell (MSC) secretome have emerged as promising alternatives, but their translation is hindered by instability, reliance on excipients, and restricted administration routes. We developed Prime-LS, a next-generation, cryoprotectant-free, lyophilized MSC-derived secretome produced through a standardized downstream process. Prime-LS retains the full secretome composition, including anti-inflammatory mediators such as galectin-9 and interleukin-1 receptor antagonist, while remaining fully soluble and biocompatible. In vitro, Prime-LS potently suppressed mitogen-induced proliferation of human PBMCs. In vivo, daily subcutaneous administration in a dextran sulfate sodium (DSS)-induced murine colitis model achieved complete protection: treated mice maintained body weight, showed preserved mucosal architecture and colon length, and exhibited normalized cytokine levels with minimal neutrophil infiltration, comparable to healthy controls. Collectively, these findings establish Prime-LS as a potent, stable, and scalable cell-free therapy, setting a new benchmark for the treatment of UC and other immune-mediated inflammatory diseases.

**Keywords:** Prime-LS; MSC-secretome; ulcerative colitis; cell-free therapy.

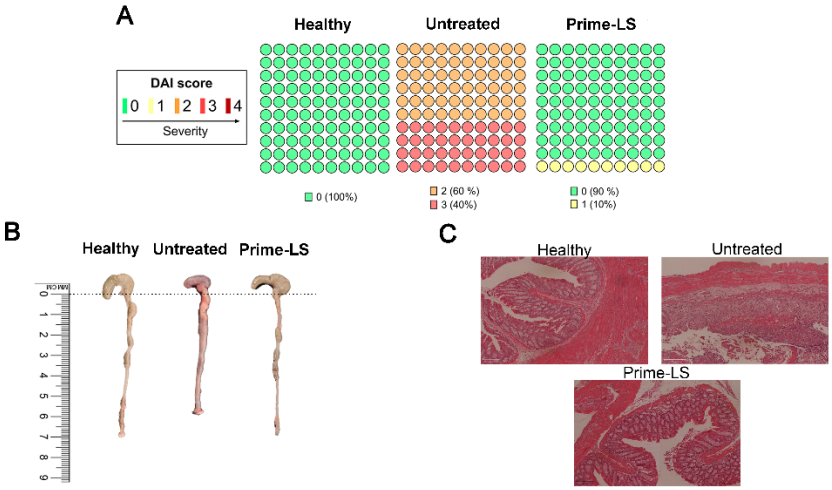


***Fig 1*. Prime-LS confers complete protection against DSS-induced colitis in vivo. (A)** Disease activity index (DAI)**. (B)** Colon length**. (C)** Representative H&E-stained sections of distal colon collected on day 7.

## Acknowledgments

This work was supported by MCIN/AEI (PID2021-122577OB-I00) and the Basque Government (IT1448-22). M. Rossello-Gelabert acknowledges funding from PRE2022-102058 (MCIN/AEI, FSE+).

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# Identification of novel antibodies against the ultraconserved MPER region of SARS-CoV-2 by phage display

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**Abstract**

In the 5 years that SARS-CoV-2 has been in circulation several variants have been selected, accumulating mutations especially in its Spike protein (S). The Spike, the main mediator of the viral entry, has been the main target for vaccines and monoclonal antibody-based therapies. However, due to the altered antigenic profiles of the Omicron variant, the virus has become resistant to most of the available therapeutic antibodies[1]. The antigenic drift of SARS-CoV-2 then hinders treatment and increases the chance of breakthrough infections. In view of the limitations of current therapeutic monoclonal antibodies, we propose targeting conserved regions of the S protein that are pivotal for infection, as is the case of the membrane-proximal external region (MPER). This strategy may provide a broader immune response that could potentially cross-react with a range of coronaviruses. In this work, we performed the biopanning of human naïve and immune scFv libraries against a soluble biotinylated MPER-derived peptide. We identified various secuences that recognize the MPER. The candidates were re-cloned into human IgG1 and expressed. Their specificity was confirmed against the soluble MPER peptide, and a MPER reconstituted in lipid vesicles to emulate a native-like exposure. Moreover, the binding kinetics of the most promising candidates were evaluated by BLI. Thus, we identified novel antibodies capable of recognizing the MPER of SARS-CoV-2, which may lead to developing broad-spectrum therapeutics against coronavirus.

**Keywords:** SARS-CoV-2, MPER, broad-spectrum antibodies, phage display.

**Graphical abstract:**

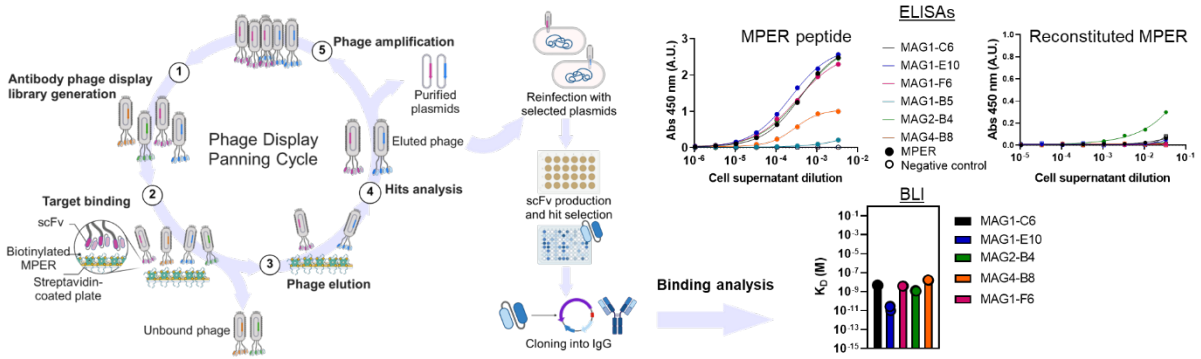


*Fig 1*. Schematics of the phage display-based IgG discovery pipeline and hit screening by Enzyme-Linked Immunosorbent Assay (ELISA) and Biolayer Interferometry (BLI).

**Acknowledgments**

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# Dynamic Biomaterials for Vascularized Engineered Tissues

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**Abstract**

The ability of living tissues to form intricate vascular networks is not a matter of chance, but the result of a finely tuned dialogue between cells and their microenvironment. At the heart of this process lies the extracellular matrix (ECM), a dynamic scaffold that does far more than provide structural support. The ECM stores, releases, and re-presents biochemical signals in a temporally and spatially controlled manner, orchestrating the growth and remodeling of blood vessels as tissues develop and repair themselves. In contrast, most tissue engineering strategies simplify this complexity by relying on static systems that release one or two growth factors in a slow and sustained manner. Such approaches may initiate early vascular sprouting, but they lack the temporal flexibility required to guide vessels through the successive stages of maturation and remodeling. The outcome is often unstable networks that fail to persist, especially when translated from controlled laboratory settings to the unpredictable environment of living systems.

In this talk, we would reimagine how engineered tissues can interact with biochemical signals. Drawing inspiration from the ECM, we put forth the idea of **dynamic biomaterials that can present multiple growth factors dynamically, allowing their availability to evolve over time**. By recreating the shifting gradients that naturally guide vascular morphogenesis, these materials provide cells with a sequence of cues that steer the formation, maturation, and stabilization of blood vessel networks.[1–3]Through this work, I demonstrate that vascular development can be more effectively controlled when tissues are provided with not just the right signals, but also at the right time and place. In doing so, this research opens the door to more physiologically relevant vascularized engineered tissues, bringing us closer to building functional constructs that integrate seamlessly with the body's own systems.

**Keywords:** Dynamic biomaterials; aptamers; growth factor; vascularization.

**Graphical abstract:**

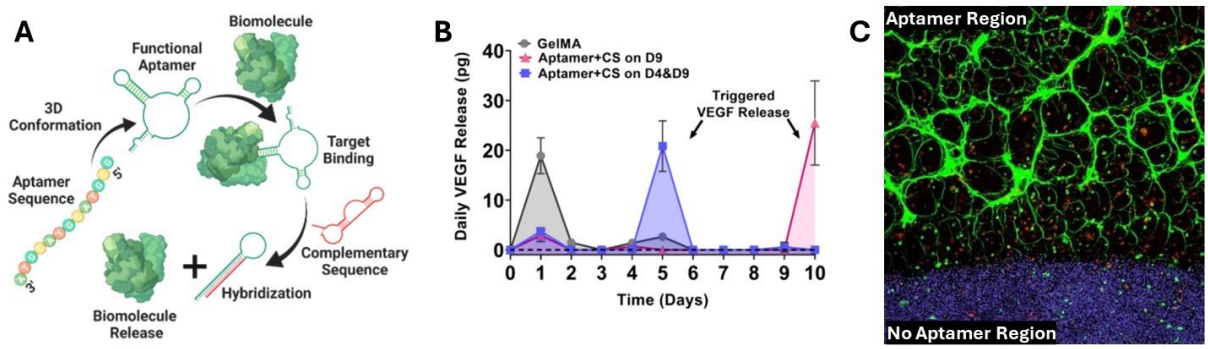


*Fig 1*. (A) Concept of aptamer-mediated growth factor sequestration and release on-demand using complementary DNA sequences as an external trigger. (B) Daily VEGF release profile from aptamer-modified hydrogels that show triggered VEGF release upon CS addition. (C) Confocal z-stack image of 3D-bioprinted construct on day 10 of culture showing interface between aptamer-modified bioinks and no-aptamer regions (GelMA bioinks) which were 3D co-cultured with MSCs and HUVECs. The image shows vascular network (green color; CD31) formation being restricted to the aptamer regions of the construct, compared to the no-aptamer regions where same initial cell densities were present.

**Acknowledgments**

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# Analysis of Protein Delivery Efficiency using GFP- and Luciferase-Loaded Extracellular Vesicles

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**Abstract**

Extracellular vesicles (EVs) are promising carriers in nanomedicine due to their biocompatibility and favorable safety profile compared with artificial nanoparticles. An innovative strategy involves loading them with therapeutic proteins through endogenous method, following the genetic modification of parental cells (1). This project aims to load EVs with a chimeric protein containing green fluorescent protein (GFP) and luciferase (Luc), to evaluate their efficiency as a drug delivery system. To achieve this, the C2C12 cell line was genetically modified, and was compared with unmodified controls (C2C12-CTRL). EVs were then produced through the endogenous pathway and isolated by centrifugation and ultracentrifugation, to obtain two subtypes: lEVs (large extracellular vesicles) and sEVs (small extracellular vesicles). Then, EVs were characterized and compared between EV-GFP/Luc (EVs from modified cells) and EV-CTRL (EVs from unmodified cells) to detect the presence of GFP and Luc. Cargo transfer was analyzed by incubating EV-GFP/Luc with C2C12-CTRL cells and tested whether the cargo was functional in the recipient cells. The fluorescent and bioluminescent properties of GFP and luciferase were used for this analysis. The results demonstrate that genetic modification of cells using the chosen endogenous method is effective without altering cell behavior. Moreover, the genetic modifications did not change EV formulation. It was also verified that EVs derived from the modified cells were loaded with GFP/Luc protein. Finally, cargo transfer experiments showed that recipient cells can internalize EVs and these vesicles could transfer functional proteins to recipient cells. Overall, EVs represent a natural, safe, and effective platform for drug delivery, with potential applications to other biological drugs such as proteins or mRNA.

**Keywords:** extracellular vesicles, GFP, luciferase, drug delivery system.

**Graphical abstract:**

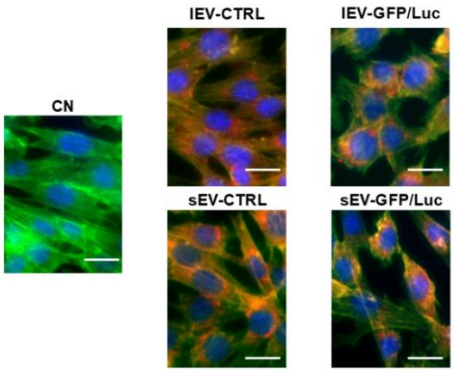


*Fig 1.* Intracellular cargo transfer assay. Fluorescence microscopy. Magnification: x40. EV: extracelular vesicle. CN: control cells without added extracellular vesicles. lEV-CTRL: large extracellular vesicles derived from control cells. lEV-GFP/Luc: large extracellular vesicles derived from modified cells. sEV-CTRL: small extracellular vesicles derived from control cells. sEV-GFP/Luc: small extracellular vesiles derived from modified cells.

**Acknowledgments**

This project was partially supported by the Basque Government (Consolidated Groups, IT1448-22).

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# II PASSION FOR SCIENCE Congress

## ORAL COMUNICATIONS
## Session IV

# Mucoadhesive Nanoparticles Based on Chitosan Derivatives for Enhanced Ophthalmic Drug Delivery

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## Abstract

Ophthalmic treatments still face significant limitations in efficacy and delivery [1]. To address these challenges, the development of nanoparticulated polymeric systems with enhanced properties is proposed, specifically mucoadhesiveness. This study focuses on a chitosan derivative soluble at ophthalmic pH and exhibiting mucoadhesive potential [2]. The nanoparticle synthesis process was optimized and characterized by particle size (100-200nm), zeta potential (13-15mV), polydispersity index (PDI) (0,2-0,4), and mucoadhesiveness through rheological and ex vivo assays. These nanoparticles can be loaded with specific ophthalmic actives to improve their bioavailability. Ectoine and ofloxacin were used as model drugs, and their release profiles were evaluated in simulated ophthalmic media.

**Keywords:** chitosan; nanoparticle; mucoadhesion; drug delivery.

## Graphical abstract:

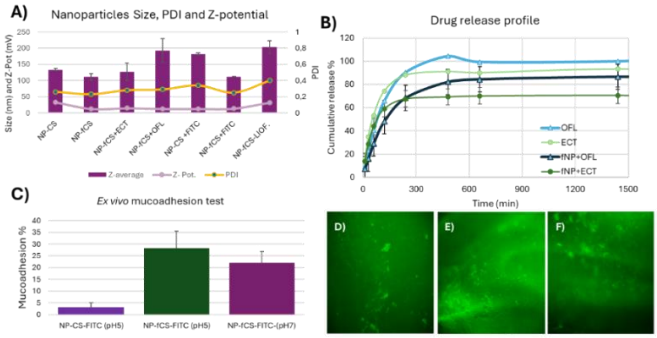


*Fig 1*. A) Comparative analysis of average Z size, PDI, and zeta potential across different nanoparticle types (n=3); B) Drug release profiles of nanoparticles loaded with ofloxacin (OFL) or ectoine (ECT) (n=3) versus free drug controls; C) Ex vivo mucoadhesion assay: fluorescence quantification expressed as % fluorescence loss upon corneal contact (n=3); D–F) Ex vivo corneal imaging after contact with chitosan nanoparticles at pH 5 (D), functionalized chitosan at pH 5 (E), and functionalized chitosan at pH 7 (F) (n=3).

## Acknowledgments

This work was supported by the Bikaintek 2022 grant (011-B2/2022, I+Med S.Coop.) of the Basque Government and the Medipol Project (EU Horizon 2020, grant No. 871650), and conducted in collaboration with Aston University, Birmingham, UK.

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# Dual Targeting of Wnt Signaling and DR5 Activation for Tumor Therapy

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**Abstract**

Glioblastoma (GBM) is a highly heterogeneous tumor, with distinct subpopulations —including cancer stem cells (CSCs)— that differ in their biology and sensitivity to cancer therapy, contributing to resistance and relapse [1]. Moreover, similar to other solid tumors, penetration of the treatment into inner regions of the tumor is highly challenging. In this work, we present a preliminary evaluation of an innovative strategy to tackle these challenges. On the one hand, addressing heterogeneity requires the development of strategies that operate through multiple mechanisms. We hypothesize that combining inhibition of Wnt signaling[2] with activation of death receptor 5 (DR5) to induce cell apoptosis[3] represents a promising dual-targeting strategy to overcome this heterogeneity. To test this, we evaluated the individual components of the approach in two different GBM cell lines with distinct characteristics. In U251 cells, anti-Frizzled antibodies led to decreased β-catenin levels and reduced Ki67 expression in both CSC and non-CSC subpopulations, demonstrating Wnt pathway inhibition. In contrast, DR5-mediated apoptosis was mainly observed in U87 cells but was less effective in U251 cells, reflecting differences in resistance mechanisms between GBM models[3]. Together, these results illustrate how targeting two different GBM cell lines with complementary vulnerabilities can help address the heterogeneity of the disease. On the other hand, we have engineered anti-Frizzled antibodies by inserting an protease-cleavable sequence into the Fv region, enabling tumor-specific release of the fragment and improved penetration into poorly accessible regions[4]. Future efforts are focused on developing bispecific antibodies that integrate effective Wnt inhibition and DR5 activation into a single therapeutic platform, aiming to provide broader antitumor coverage and a more tumor-specific strategy in GBM.

**Keywords:** Glioblastoma, Cancer stem cells, Tumor heterogenecity, Tumor penetration, Wnt signaling, DR5 activation, Fv release

**Graphical abstract:**

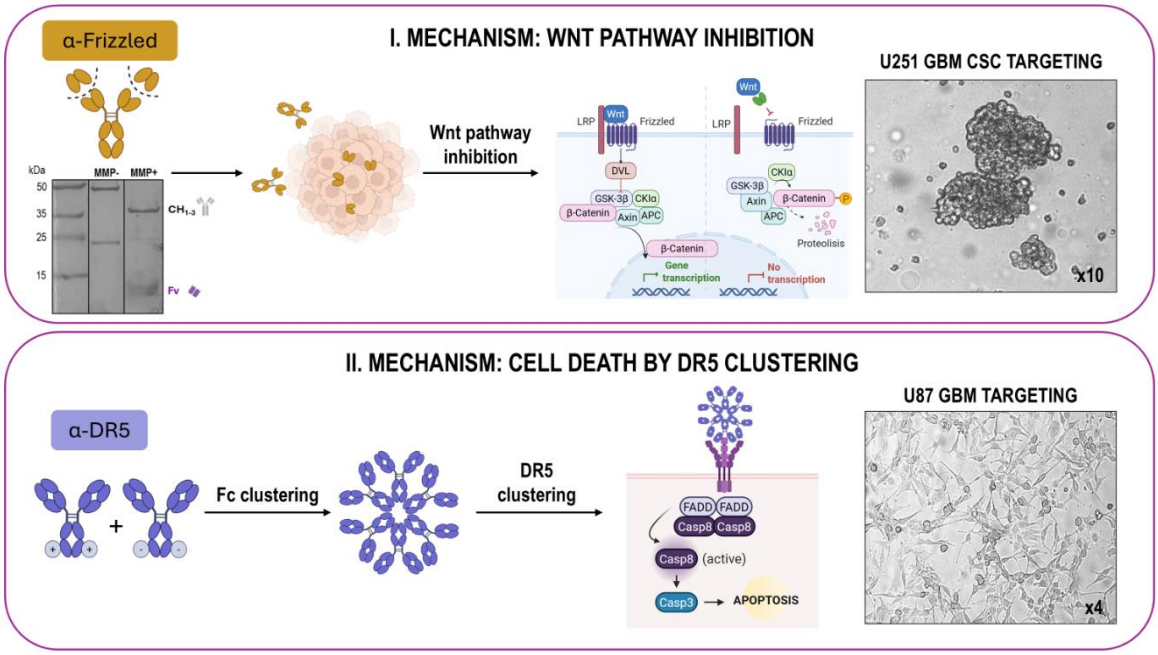


**Fig 1. Complementary targeting of GBM heterogeneity.** WT anti-Frizzled antibodies reduced β-catenin and Ki67 in U251 CSCs, while cleavage of the engineered antibody was confirmed by SDS-PAGE. Anti-DR5 antibodies induce apoptosis in U87 cells through receptor clustering.

## Acknowledgments

This work was supported by The Worldwide Cancer Research organization (Grant 25-0158) and MICIU/AEI/ 10.13039/501100011033 and “ERDF A way of making Europe” (Grant PID2021-122212OA-I00).

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# Complement factor H gene supplementation therapy for dry age-related macular degeneration

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**Abstract**

Dry age-related macular degeneration (dAMD) is a retinal disease marked by degeneration of the retinal pigment epithelium (RPE), leading to vision loss and irreversible blindness. Its pathogenesis is strongly linked to complement cascade dysregulation, which has emerged as a novel therapeutic target [1]. Complement factor H (CFH) or its smaller isoform, factor H–like protein 1 (FHL-1) are key inhibitors of C3 convertase in the complement cascade. The insufficiency of these proteins is related to an early-onset macular degeneration. Gene supplementation of CFH or FHL-1 would provide sustained *de novo* production of these proteins by retinal cells [2]. To achieve this goal, nanodelivery systems for intravitreal administration of nucleic acids based on solid lipid nanoparticles (SLNs), protamine and dextran (Dx) have been designed and evaluated in human retinal pigment epithelial (ARPE-19) cells. Formulation factors, including the method of preparation, lipid composition and pH, were studied. Lipid-based non-viral vectors contained the reporter gene pcDNA3-GFP (green fluorescent protein) or the therapeutic plasmids pDNA-CFH or pDNA-FHL-1. Nanoformulations presented optimal physicochemical characteristics (100-300 nm; pdi < 0.4; surface charge +28 to +57 mV), and capacity to bind, protect, and release the pDNAs tested. The higher transfection levels were archieved with SLNs containing the ionizable lipid DODAP and prepared by the solvent emulsification-evaporation technique. No differences were observed between formulations prepared either at pH 7 or pH 4.5. A cellular model of oxidative stress similar to AMD was developed in ARPE-19 cells by adding different concentrations of hydrogen peroxide ($H_2O_2$). Cell viability was assessed via MTT assay at 24 and 48 hours after transfection. Genetic supplementation with CFH and FHL-1 provided protective effects against oxidative stress. In conclusion, nanovectors designed showed high transfection efficacy and suitable features for ocular administration, paving the way for a further in vivo evaluation as retinal delivery systems.

**Keywords:** pDNA; nanovectors; retina, complement system.

**Graphical abstract:**

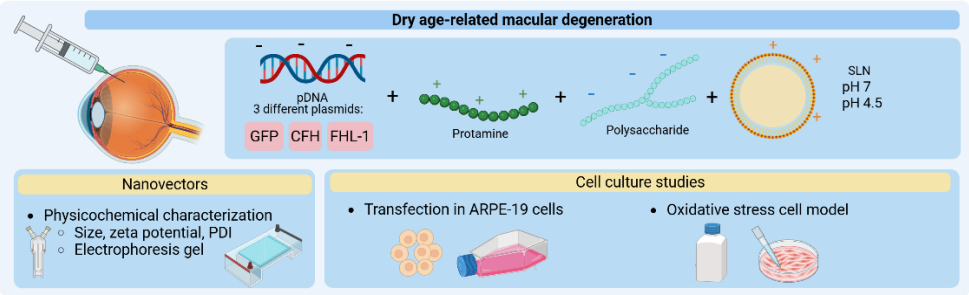


*Fig 1*. Formulation and characterization of nanovectors and cell culture studies in ARPE-19 cells.

**Acknowledgments**

P. Fernández-Muro and M. Arribas-Galarreta thank the University of the Basque Country UPV/EHU (PIFG23/45) and the Basque Government (PRE_2022_1_0144) for their research grants. This work was founded the MCIU/AEI/FEDER, UE (PID2022-139800OB-I00) and by Basque Government (IT1587-22).

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# Development of a colon-targeted delivery system for mesenchymal stromal cell-derived secretome in inflammatory bowel disease

Camino Garcia-Blasco [1,3,*], Maria Rossello-Gelabert [1,3], Manoli Igartua [1,2,3], Edorta Santos-Vizcaino [1,2,3] and Rosa Maria Hernandez [1,2,3].

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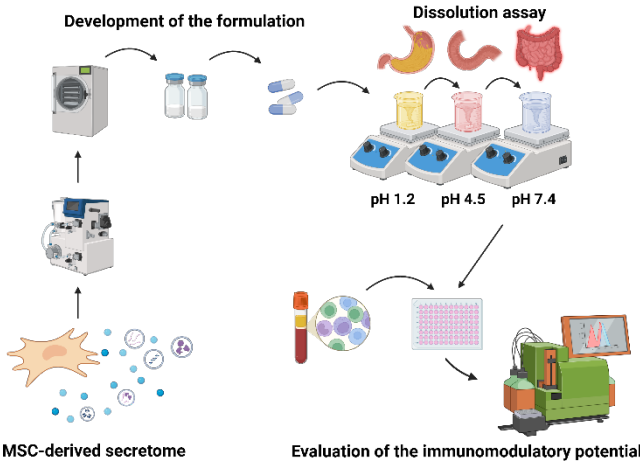
**Abstract**

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of the gastrointestinal (GI) tract whose rising incidence, limited therapeutic options, and severe complications highlight the need for more effective and targeted therapies [1]. In this study, we developed a colon-specific immunomodulatory delivery system based on bioactive factors secreted by mesenchymal stromal cells (MSCs). To this end, hair follicle-derived MSCs (HF-MSCs) were cultured and subjected to an optimized inflammatory preconditioning protocol [2], generating an immunomodulatory secretome. This was subsequently isolated, purified, and lyophilized through a proprietary downstream process. The resulting product, termed Prime-LS, was encapsulated and coated with a pH-responsive polymer to enable oral administration and targeted colonic release. The system was evaluated using dissolution assays in media simulating GI conditions and a functional assay with activated peripheral blood mononuclear cells (PBMCs), labeled with CFSE to monitor their proliferation. The ability to withstand acidic conditions, together with the effective suppression of activated PBMCs proliferation, demonstrated both the robustness of the formulation and the immunosuppressive potential of the released Prime-LS.

**Keywords:** inflammatory bowel disease, mesenchymal stromal cells, secretome, colonic delivery.

**Graphical abstract:**




**Acknowledgments**

This work was supported by Grant PID2021-122577OB-I00 (MCIN/AEI/ 10.13039/501100011033), "ERDF A way of making Europe", and by Grant IT1448-22 from the Basque Government. C. García-Blasco acknowledges a predoctoral grant from Eusko Jaurlaritza (PRE_2024_2_0058) and M. Rossello-Gelabert a grant PRE2022-102058 (MCIN/AEI/10.13039/501100011033 and FSE+).

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# II PASSION FOR SCIENCE Congress

# POSTER COMUNICATIONS

# Stability of added *gamma*-oryzanol during sunflower oil heating at frying temperatures: kinetics and degradation products

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## Abstract

Compounds with potential antioxidant capacity are often added to increase oil stability during food thermal processing. *Gamma*-oryzanol, a mixture of ferulic acid esters of triterpene alcohols/sterols from rice bran is considered a radical scavenger but its ferulates degrade upon heating [1]. Thus, understanding their fate during common thermal processing is crucial. However, limited research has been addressed on this subject and even less regarding the characterization of their degradation products. In this context, *gamma*-oryzanol (0.5 and 1%) was added to sunflower oil and heated at 170 °C without food. Its degradation was monitored by Proton Nuclear Magnetic Resonance spectroscopy ($^1$H NMR), while the resulting degradation products were identified using Direct Immersion Solid-Phase Microextraction followed by Gas Chromatography-Mass Spectrometry (DI-SPME-GC/MS).
$^1$H NMR results showed that, regardless the level of enrichment, triterpenyl alcohol and steryl ferulates exhibited first-order degradation kinetics. The generation of six compounds derived from the feruloyl moiety was observed by DI-SPME-GC/MS. These were mainly vanillin, followed by acetovanillone, 4-vinylguaiacol, scopoletin, 4-methylguaiacol, and guaiacol. Free triterpernic alcohols and sterols were also detected, but their abundances did not increase, possibly because their degradation rate exceeded that of their formation.

**Keywords:** *gamma*-oryzanol, sunflower oil, $^1$HNMR, DI-SPME-GC/MS

**Graphical abstract:**

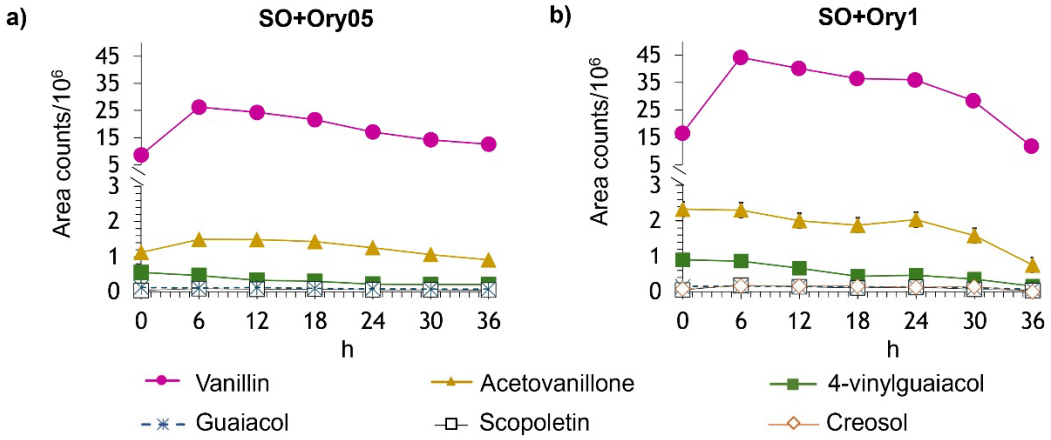


*Fig 1*. Evolution of the abundances of *gamma*-oryzanol thermodegradation products in enriched sunflower oils at a) 0.5% (SO+Ory05) and at b) 1% (SO+Ory1) along the heating experiment.

## Acknowledgments

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# [6]- and [7]-Helicenic Diols as Scaffolds for the Synthesis of a New family of Chiral Brønsted Acids

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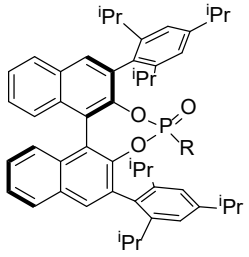
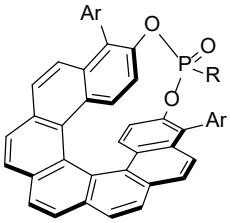
**Keywords**: *Helicenes, Chiral Brønsted Acids, Asymmetric organocatalysis*

Since the beginning of the 21st century, asymmetric organocatalysis has emerged as a new tool enabling the selective synthesis of complex organic molecules.[1,2] This field of research aims to find an alternative to the use of toxic metal salts by using small chiral organic molecules acting as asymmetric catalysts in enantioselective transformations. Among the families of asymmetric organocatalysts developed, chiral Brønsted acids play a prominent role due to their ability to activate a wide variety of electrophiles and induce a large array of highly enantioselective reactions. In this context, BINOL-based catalysts are described as the main family allowing reactions using simple and mild conditions, due to their high versatility.[3,4]

In order to access this new family of Brønsted acid organocatalysts possessing a chiral helicenic diol in its backbone and a phosphoric acid or phosphoramide moiety as acidic centre, a 13-step synthesis has been developed for the asymmetric synthesis of chiral [6]- and [7]-helicenic diols.[5] Efforts toward the synthesis of the Brønsted acids will be discussed.




R= OH, NHTf




R= OH, NHTf

## Acknowledgments

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Poster

# GENERATION AND COMBINATION OF IONOGEL MICROSTRUCTURES USING VACUUM-DRIVEN LITHOGRAPHY TECHNIQUE

Juncal Alonso-Cabrera[1,2], Enrique Azuaje-Hualde[1], Alexia Ramos-Gutiérrez[1,2], Mikel Diez-Bravo[1,2], Fernando Benito-Lopez[2*] and Lourdes Basabe-Desmonts[1,3*]
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This work introduces a novel application of vacuum-driven lithography for the efficient fabrication of high-resolution, homogeneous, multifunctional ionogel microstructures. For the first time, we demonstrate the simultaneous generation and combination of ionogels microstructures with varying physicochemical properties in a single loading and polymerization step. Furthermore, the integration of a pH-sensitive dye enables the fabrication of robust, miniaturized colorimetric sensors with a detection range from pH 3 to 12, advancing the versatility of ionogel-based sensing platforms [1].

This technique addresses the gap of the current fabrication methods such as solvent casting, inkjet printing and electrospinning as they face limitations in scalability, uniformity, resolution, and material compatibility. Many of these methods require labor-intensive preparation, lack the ability to create intricate microstructures, or are restricted in their capacity to integrate multiple ionogel compositions within a single step [2]. Vacuum-driven lithography offers a promising solution to these challenges as it enables precise, scalable patterning of ionogels with varying properties on the same surface while maintaining control over microstructure dimensions and composition. This method could not only improve precision and reproducibility but also facilitate the creation of complex, multi-material systems through a straightforward process.

Vacuum-driven lithography involves degassing polydimethylsiloxane (PDMS) molds under vacuum, creating a negative pressure environment [3]. Upon restoring atmospheric pressure, ionogel precursors are drawn into intricate microchannel designs within the molds, followed by photopolymerization using UV light (Figure 1). Ionogel microstructures were fabricated using three ionic liquids: EMIES, DCA, and choline acetate. Profilometry confirmed consistent structural heights ranging from 17 to 24 μm with excellent intra- and inter-microstructure homogeneity, particularly at the optimized 20-cycle UV exposure (Figure 2). The method facilitated the combination of ionogels with different compositions within a single substrate, creating multi-functional designs (Figure 3). The combined structures maintained high resolution and functionality, showcasing the versatility of the technique (Figure 4). A proof-of-concept pH sensor was developed by incorporating bromocresol purple into the ionogel matrix, yielding a robust and reproducible colorimetric response, capable of detecting a wide pH range from 3 to 12 within seconds (Figure 5). The integrated pH sensor displayed color changes from yellow (acidic) to blue (alkaline), with a measurable shift in pKa, from 6.3 in solution to 4.9, attributed to immobilization effects. Calibration curves demonstrated reliable sensing performance, with inter-replicate variations due to microstructure uniformity.

Therefore, vacuum-driven lithography is demonstrated to be a transformative technique for fabricating high-resolution, multifunctional ionogel microstructures. By enabling the simultaneous integration of ionogels with diverse physicochemical properties, this method offers unprecedented versatility for designing advanced microdevices. The incorporation of a pH-sensitive dye further highlights the potential of ionogels as robust, miniaturized sensing platforms with wide-ranging applicability in environmental monitoring, biomedical diagnostics, and wearable technologies [5]. These results establish vacuum-driven lithography as a scalable, precise and efficient fabrication method, paving the way for the development of next-generation ionogel-based devices with customizable functionalities.

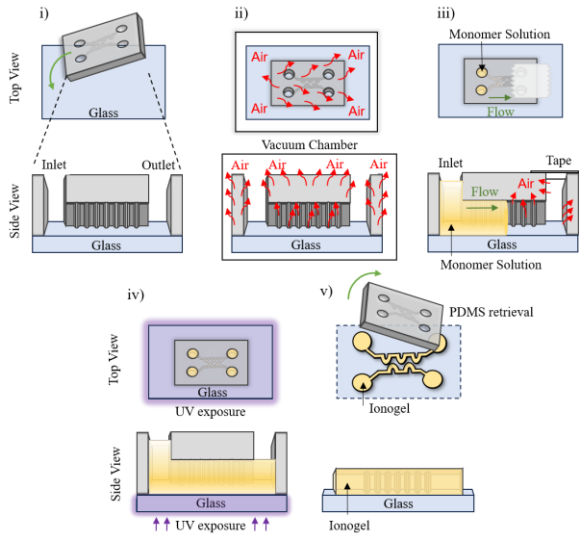


*Figure 1: Schematic representation of the generation of microstructures by vacuum-driven lithography showing the top and side view.*

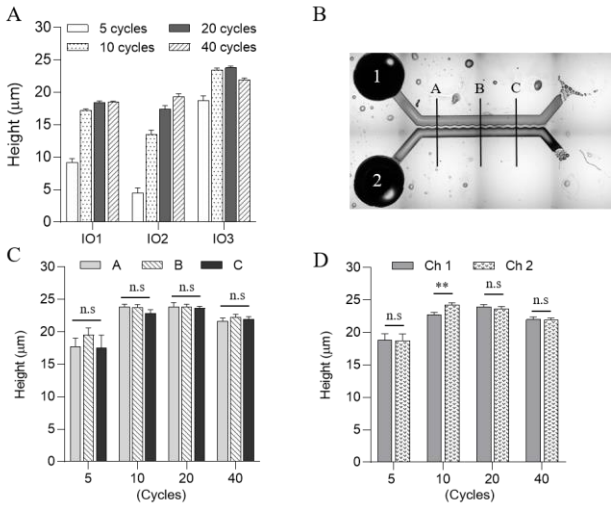


*Figure 2: Generation of ionogel microstructures. A) Graphic of the height obtained of the ionogel microstructures generated by UV light exposure measured with a contact profilometer. B) Representation of the microstructure design with the channel (1 and 2) and the regions (A, B and C). C) Graphic of the height of the different sections of the generated IO3 microstructures D) Graphic of the height of each channel (Ch) of the generated IO3 microstructures.*

## ACKNOWLEDGEMENTS

We acknowledge funding support from Basque Government, under Grupos Consolidados with Grant No. IT1633-22 and 'Ministerio de Trabajo y Economía Social' under the "Investigo" program financed by Lanbide-Servicio Vasco within the European Union NextGenerationEU/PRTR funds.

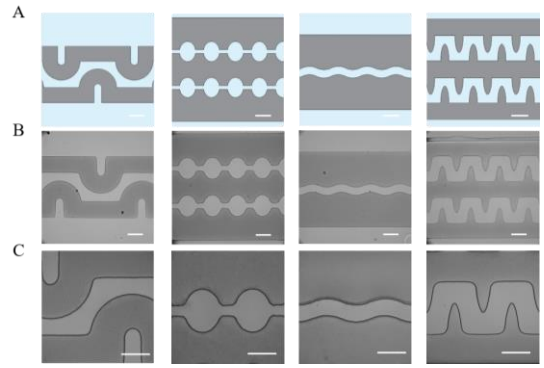


*Figure 3. IO1 microstructures. A) Representation of four different microstructure designs. B and C) Brightfield images of glass substrates with four different ionogel microstructure designs. Scale bars represent 200 µm.*

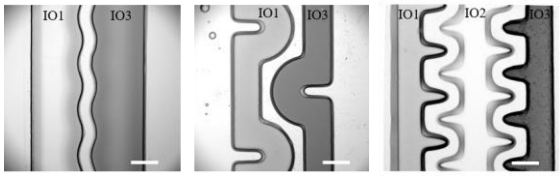


*Figure 4: Combination of ionogel microstructures. Brightfield images of glass substrates with different ionogel microstructures combination. Scale bars: 200 µm.*

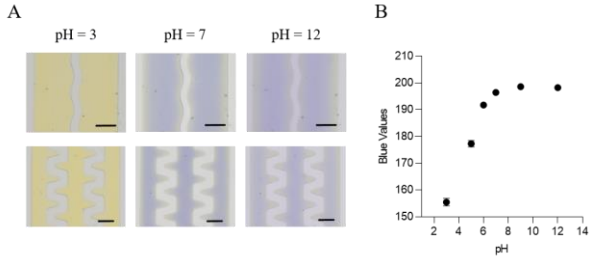


*Figure 5: Combination of IO3 microstructures with pH indicator (bromocresol purple) colorimetric sensor. A) Brightfield images of ionogel microstructures for three different pH conditions (3, 7 and 12). Scale bars represent 200 µm. B) Blue values for the ionogel with BCP indicator used as colorimetric sensor, when varying the pH from 3 to 12. Error bars mean SEM (n = 45 per condition).*

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# Guidelines on abstract format for submission to the II Congress "Passion for Science"

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## Abstract

*Staphylococcus aureus* is a major pathogen in the dairy industry, associated with bovine mastitis and contamination of milk and cheese products. Its ability to form biofilms, produce enterotoxins, and develop antimicrobial resistance makes it difficult to control. In this study, ten lytic bacteriophages specific to *S. aureus* were isolated from environmental and livestock samples in the Basque Country. Transmission electron microscopy revealed that the phages had tailed morphologies typical of the class *Caudoviricetes*, and quantitative PCR confirmed the molecular identity of one phage within the *Herelleviridae* family. The most effective phages were combined into cocktails and tested against *S. aureus* in both tryptic soy broth and skim milk, achieving significant reductions in bacterial counts of up to 9–11 log in milk. These findings demonstrate the potential of bacteriophages as a safe, sustainable, and effective biocontrol strategy against *S. aureus* in dairy environments*

**Keywords:** *Staphylococcus aureus*, bacteriophages, dairy industry, biocontrol.

## Graphical abstract:

The figure shows that both individual bacteriophages and a phage cocktail reduced *Staphylococcus aureus* in tryptic soy broth. Phage cocktails were the most effective, achieving up to 7-8 log reductions in broth and 9-11 log in skim milk, demonstrating their potential as powerful biocontrol agents in laboratory and food environments.

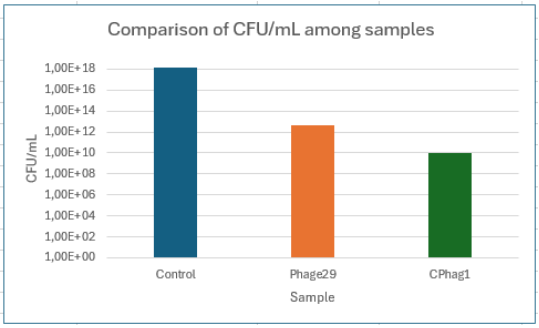


*Fig 1*. Reduction of *Staphylococcus aureus* through treatment with individual bacteriophages and a phage cocktail

## Acknowledgments

This work was supported by MikroIker, whose funding and resources made this study possible. We also thank SGIKER for their valuable technical support and guidance throughout the project. Special thanks to the Microbiology Department for providing laboratory facilities and equipment.

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# Sexual dimorphism in the treatment of rats with *Opuntia strica* var. *dillenii* fruit extract to prevent obesity and related co-morbidities

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**Abstract**

Research involving females is limited, and this gap may have important ethical implications. Sexual dimorphism is influenced by multiple factors, including differences in organ and tissue development, as well as variations in the availability of sex hormones and their receptors [1]. *Opuntia stricta* var. *dillenii* (OD) fruit is rich in bioactive compounds such as betalains, flavonoids, and phenolic acids, which have demonstrated beneficial effects in the prevention and treatment of various diseases, including obesity [2, 3]. This study aimed to investigate the preventive effects of a whole-fruit OD extract on obesity and related co-morbidities. Sixty Wistar rats (30 females (F) and 30 males (M)) were allocated into control groups fed a standard diet (CF, CM), obese control groups fed a high-fat high-fructose (HFHF) diet (OF, OM), and experimental groups fed the HFHF diet supplemented with 75 mg/kg/day of whole fruit OD (EF, EM). The experimental period lasted 8 weeks, with *ad libitum* access to food and water. Body weight and food intake were recorded daily. At the end of the study, animals were sacrificed under anesthesia, blood was collected via cardiac exsanguination, and liver and adipose tissues were dissected. Serum triglycerides, glucose, and cholesterol levels were measured by spectrophotometry, while insulin levels were analysed using an ELISA kit. No significant differences in final body weight were observed between obese control and experimental groups in either sex, and serum glucose and cholesterol levels remained unchanged. In females, the extract reduced liver weight and insulin levels compared to the OF group, whereas these parameters were unaffected in males. Conversely, the extract decreased serum triglycerides levels and perirenal and subcutaneous adipose tissue weights in males, while these parameters remained unchanged in females. These findings indicate that the OD extract exerts sex-specific effects, thereby confirming sexual dimorphism. Further research is required to elucidate the mechanisms of action and the pathways involved. Overall, administration of the OD extract may be beneficial for the prevention of obesity in males and the prevention of steatosis in females.

**Keywords:** *Opuntia stricta* var. *dillenii*, sexual dimorphism, obesity, steatosis.

**Graphical abstract:**

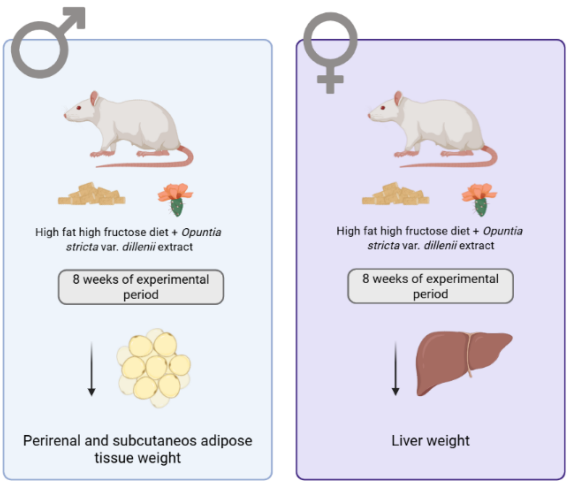


*Fig 1*. Results of *Opuntia stricta* var. *dillenii* extract in male and female rats fed a high-fat high-fructose diet.

**Acknowledgments**

Helen Carr-Ugarte is the recipient of a predoctoral fellowship from the University of the Basque Country (PIF2022/95).

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# Preventive effect of *Opuntia* extracts in steatosis and autophagy in a murine model of diet-induced liver disease

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**Abstract**

Metabolic dysfunction-associated steatotic liver disease (MASLD) is characterized by excessive hepatic fat accumulation, which may be prevented by bioactive compounds present in plants. This research aimed to analyze the effectiveness of extracts from two *Opuntia* species, rich in polyphenols and betalains [1, 2], in steatosis prevention and their role in both hepatic lipid metabolism and autophagy. Sixty male Wistar rats were separated into 6 groups and given either a standard (C) or high-fat high-fructose (HFHF) diet, supplemented with or without 25 or 100 mg/kg/day of *Opuntia stricta* var. *dillenii* peel extract (L-OD and H-OD, respectively), or *Opuntia ficus-indica* var. *colorada* pulp extract (L-OFI and H-OFI, respectively), over a period of 8 weeks. Hepatic triglycerides were quantified spectrophotometrically, while the degree of steatosis was assessed through histological analysis. The protein expression of fatty acid synthase (FAS), acetyl-CoA carboxylase (pACC/ACC), unc-51 like autophagy activating kinase 1 (pULK1/ULK1), microtubule-associated protein 1A/1B-light chain 3 (LC3) and sequestosome-1 (p62) was analyzed by Western blot. At the end of the experimental period, the HFHF group showed hepatic steatosis. In the L-OFI group, hepatic triglyceride content was significantly lower than in the HFHF group. The other groups showed no effect. The HFHF diet caused a reduction in pACC/ACC ratio (index of ACC activity) and an increase in FAS protein expression, indicating higher *de novo* lipogenesis. Regarding autophagy, phosphorylation of ULK1 at serine 757 inhibits this protein and consequently autophagy. Thus, the HFHF group showed an activation of autophagy since a decrease in pULK1/ULK1 ratio was observed. Moreover, an increase in LC3II/LC3I ratio and in p62 protein expression was reported in the HFHF group. L-OFI supplementation demonstrated a trend towards higher pACC/ACC ratio ($p$=0.08) and was able to significantly reduce FAS expression. H-OFI increased pACC/ACC, and both L-OD and H-OD groups decreased FAS protein expression. Regarding autophagy, L-OFI was the only treatment able to partially prevent the diet-induced reduction in pULK1/ULK1 ratio. L-OFI also showed a tendency towards lower values in LC3II/LC3I ratio ($p$=0.1) and p62 protein expression ($p$=0.09), compared to HFHF group. The oter groups treated with *Opuntia* extract did not show a regulation of these parameters. In conclusion, L-OFI supplementation partially prevented steatosis by downregulating *de novo* lipogenesis and autophagy. OD extract improved parameters related to *de novo* lipogenesis, but this was not sufficient to prevent steatosis.

**Keywords**: *Opuntia*, steatosis, *de novo* lipogenesis, autophagy.

**Acknowledgments**

This work was supported by the Ministry of Science and Innovation, project number PID2020-118300RB-C22 and a FPI predoctoral grant.

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# DEVELOPMENT OF HYDROGEN SULPHIDE-ACTIVATED THERAGNOSTIC PRODRUGS FOR SELECTIVE CANCER TREATMENT THROUGH TETRAZINE DYNAMIC CHEMISTRY

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A novel approach for the synthesis of hydrogen sulphide ($H_2S$) activated theragnostic prodrugs is the dynamic nucleophilic aromatic substitution of tetrazines. The dynamic covalent chemistry of tetrazines provides a reversible and environmentally sensitive system, ideal for targeted release of therapeutic products. Therefore, it becomes a targeted administration in cancer therapy with the objective of mitigating adverse effects and improving the efficiency of the drugs.[1] Overexpression of $H_2S$ in cancer cells, such as colon cancer, triggers the release of the therapeutic agent camptothecin, a naturally topoisomerase inhibitor known for its instability, which this self-immolative system aims to stabilise, along with a fluorescent marker.[2] This dual release mechanism not only promises greater selectivity towards malignant cells, but also allows the compound to be tracked, marking an important step forward in theragnostic therapy applications.[3] It is worth highlighting the potential of tetrazine-based systems in the development of sensitive and selective therapeutic solutions, particularly for conditions marked by elevated $H_2S$ levels. This strategy opens up to incorporate a variety of cytotoxic agents and luminescent probes, expanding the scope for innovative modalities to detect and treat cancer and other $H_2S$-related diseases.

**Keywords:** cancer, self-immolative, camptothecin, topoisomerase

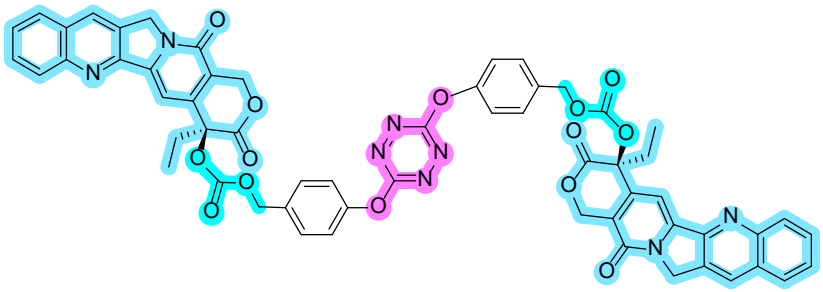

Figure 1. Chemical structure of self-immolative system based on tetrazine.

**Acknowledgments**

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# Design of Treg-targeted nanoparticles for cancer treatment

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## Abstract

Nanoparticles have emerged as a key tool in pharmaceutical development due to their ability to enhance the solubility and stability of therapeutic compounds, prolong their half-life, and enable controlled drug release. Their versatility also allows for surface modification with polymers or ligands, optimizing biodistribution and minimizing adverse effects by directing the drug toward specific tissues or target cells.

In oncology, their application is particularly relevant, as they facilitate selective accumulation within the tumor microenvironment and enable the delivery of agents that modulate immune responses, primarily through the Enhanced Permeability and Retention (EPR) effect [1].

Cancer immunotherapy aims to elicit robust antitumor responses from $CD8^+$ T cells while counteracting resistance mechanisms driven by the tumor microenvironment (TME). In this context, suppressing the pro-tumoral activity of regulatory T cells (Tregs) represents a promising and innovative strategy [2]. This study presents the design and characterization of Treg-targeted nanoparticles capable of improving treatment stability and enhancing the efficacy of immunotherapy in preclinical cancer models. The formulation achieves complete anti-timor responses in combination therapies, using doses up to 50 times lower than those required for the free compound [3].

**Keywords:** Liposome, Treg cells, oncology, translation approach

## Graphical abstract:

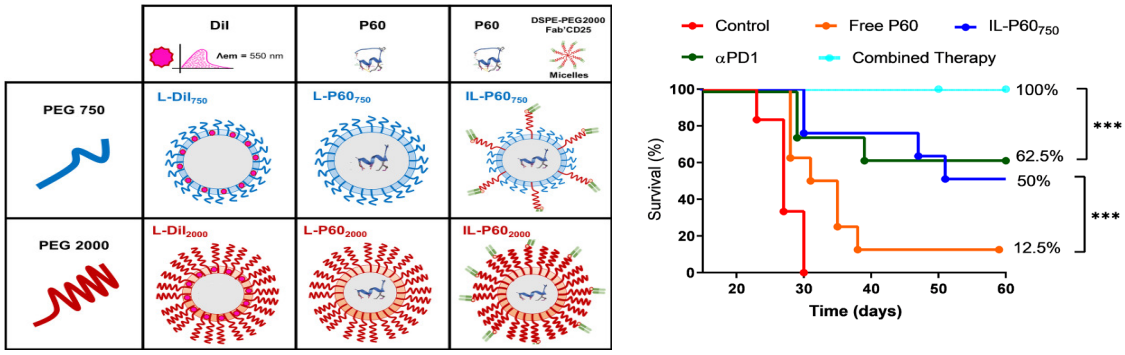


*Fig. 1.* Encapsulated peptide formulations and anti-tumor efficacy. Several coating and targeting strategies were evaluated to select the final formulation, which elicited complete responses in tumor models.

## Acknowledgments

This work was supported by the FPU grant [ref. BOE-B-2023-39522] awarded by the Spanish Ministry of Universities.

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# Evaluation of biosurfactant-producing halophilic bacteria for the bioremediation of oil-contaminated sands

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**Abstract**

Halophilic microorganisms, thriving in extreme environments, produce valuable compounds such as antimicrobials and biosurfactants, which hold significant promise for industrial, pharmaceutical, and environmental applications. This study aims to investigate the biosurfactant production capacity of a collection of halophilic bacterial isolates, utilizing glycerol as a carbon source. Additionally, the study evaluates the bioremediation potential of the extracted biosurfactants in the remediation of sand contaminated with used cooking oil (UCO) and used motor oil (UMO). Biosurfactant production was assessed through emulsion assays (E24 index), Oil Spreading, and Parafilm-M tests. The isolates ASV58 and ASV77T were selected based on their positive results, making them suitable candidates for biosurfactant extraction. The extraction was performed using cold ethanol precipitation followed by dialysis for purification, ensuring high-quality biosurfactant isolation [1]. The efficacy of the biosurfactants in environmental remediation was tested by applying their solutions to sand samples contaminated with UCO and UMO, with oil removal quantified by gravimetric analysis [2]. A total of 24 isolates were identified as effective biosurfactant producers. The biosurfactant extract from ASV77T exhibited remarkable efficiency, achieving over 64% oil removal for both UCO and UMO, while ASV58 also demonstrated notable performance with removal efficiencies exceeding 59%. Based on these results, further studies will be conducted to expand upon these findings.

**Keywords:** halophiles, biosurfactants, contaminated sand, oil removal

**Graphical abstract:**

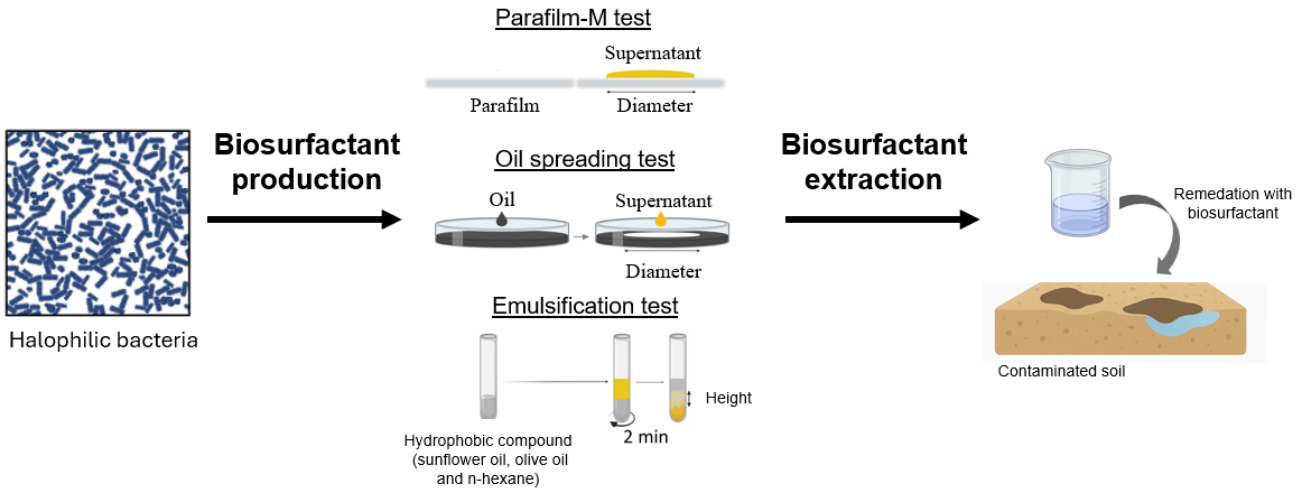


*Fig 1*. Halophilic biosurfactants for oil-contaminated sand remediation

**Acknowledgments**

This work was supported by UPV/EHU (GIU 21/021), Basque Government (PIBA_2023_1_0036) and the Añana Salt Valley.

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# Extracellular Vesicles as Biologic Drug Delivery Systems: Pharmacokinetic Advantages over Soluble Forms

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**Abstract**

Biologic-based therapeutics hold great promise for treating numerous diseases. However, they face limitations related to instability and on-target off-tissue adverse effects [1]. Erythropoietin (EPO), widely used to treat anemia, exemplifies these challenges, as its intermittent high-dose administration may cause iron deficiency and cardiovascular complications [2]. Extracellular vesicles (EV) have emerged as advanced drug delivery systems capable of protecting biologics, prolonging circulation, and enabling controlled release [3]. In the present work, we evaluated the pharmacokinetics of EPO-loaded EV (large EV, lEV; and small EV, sEV) compared with free soluble EPO following intravenous (IV), intraperitoneal (IP) and subcutaneous (SC) administration in mice. Control mice received PBS to establish baseline EPO levels. Free EPO exhibited rapid absorption, peaking at 6 h after IP and SC administration, but levels declined to baseline by 24 h. IV administration resulted in a more rapid decline in plasma levels, with no significant differences from controls after 2 h. After IV administration of EV, EPO levels remained very low (<250 pg/mL), similar to baseline, throughout the entire sampling period. In contrast, EV-based formulations administer through SC and IP routes displayed delayed kinetics, with peak plasma concentrations at 24 h. After IP administration, EPO plasma levels were higher with lEV than with sEV, whereas no difference was observed after SC administration. Moreover, at 48 h, only the SC groups showed EPO levels above baseline. Dose-escalation studies confirmed that medium and high doses of lEV and sEV maintained elevated levels up to 72 h, whereas lower doses were insufficient. These results demonstrate that EV encapsulation confers a sustained and route-dependent pharmacokinetic profile to EPO. Notably, this profile also depends on the EV subtype and their biogenesis mechanisms. In conclusion, EVs represent a promising platform for biologic drug delivery, offering pharmacokinetic advantages over soluble formulations by reducing variability, extending drug exposure, and potentially improving the safety and efficacy of current therapies.

**Keywords:** extracellular vesicles, biologic drug delivery, pharmacokinetics, erythropoietin.

**Graphical abstract:**

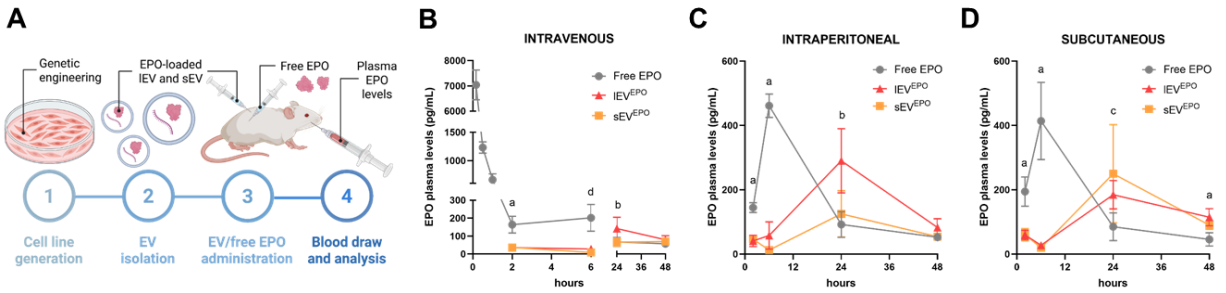


*Fig 1. A. Workflow schematic. B,C,D. EPO plasma levels after IV (B), IP (C) and SC (D) administration of free EPO and EPO-loaded EV. a → EPO ≠ (Large = Small); b → (EPO = Small) ≠ Large; c → (EPO = Small) (Large = Small) (Large ≠ EPO); d → EPO ≠ Large ≠ Small; no letter → no significant differences.*

**Acknowledgments**

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# Population pharmacokinetic modeling of piperacillin administered as extended infusion in critically ill patients

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**Abstract**

Piperacillin/tazobactam is a beta-lactam/beta-lactamase inhibitor combination with activity against gram-positive and gram-negative aerobic and anaerobic bacteria [1]. This work aimed to develop a population pharmacokinetic model of piperacillin in critically ill patients after its administration as a 4-hour infusion. The study was carried out at the Araba University Hospital (Vitoria-Gasteiz). The patients received a dose of 4/0,5 g of piperacillin/tazobactam q6h as a 4-hour infusion. Five plasma samples of each patient were collected at steady state at different times over a dosing interval, and drug concentration was quantified using a validated HPLC-UV technique. Nonlinear mixed-effects modeling was performed using NONMEM 7.5, applying first-order conditional estimation method with interaction (FOCE+I). Piperacillin plasma concentration-time data from 24 patients were best described by a one-compartment model. The residual error was estimated using a combined error model. Different covariates were explored, but the final model only retained the creatinine clearance (CrCL) and body weight as covariates for clearance (CL) and distribution volume (V), respectively. Parameter estimates (%RSE) were 20.5 L (8.1%) for V and 11.7 L/h (6.8%) for CL. Between-subject variability (IIV) estimates for the V and CL were 11.3% (82.4%) and 30.2% (14%), respectively. The results of the bootstrap indicated a good precision of the final model parameter estimates and an adequate model stability. This model will be usefull for PK/PD analysis and Monte Carlo simulations to estimate the probability of attaining the pharmacokinetic/pharmacodynamig target, and thus, the likelihood of treatment success.

**Keywords:** population pharmacokinetic modeling; critically ill patients; piperacillin.

**Graphical abstract:**

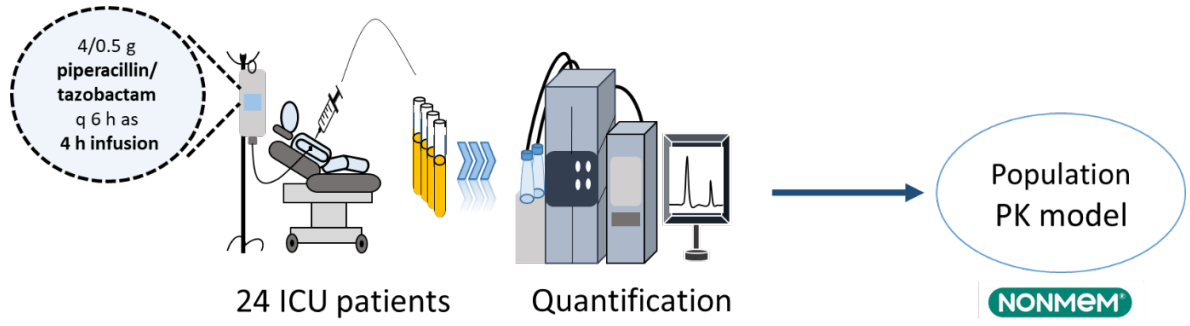


*Fig 1*. Workflow for the development of the population pharmacokinetic model

**Acknowledgments**

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# ✓Autonomous paper valves using pdms vacuum pumps as actuators for colorimetric chrono-sampling

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**Abstract**

Paper-based microfluidic devices (μPADs) are low-cost, portable platforms ideal for point-of-care (POC) diagnostics and field testing [1]. An autonomous device combining colorimetric sensors and paper-based valves was developed for chrono-sampling applications, preserving tan simplicity of paper-based microfluidic devices (μPADs). The paper valve is actuated by a passive vacuum pump made of air-permeable PDMS, whose channel geometry was modified to control permeability and activation time. The PDMS pump was experimentally characterized and modeled through numerical simulations to optimize its performance. As proof of concept, the device was used to monitor the pH profile of culture media at four time points, each 45 minutes apart, demonstrating its potential for simple, time-resolved chemical analysis.

**Keywords:** Paper-based microfluidics (μPADs), Autonomous chrono-sampling, PDMS vacuum pump Colorimetric sensing.

**Graphical abstract:**

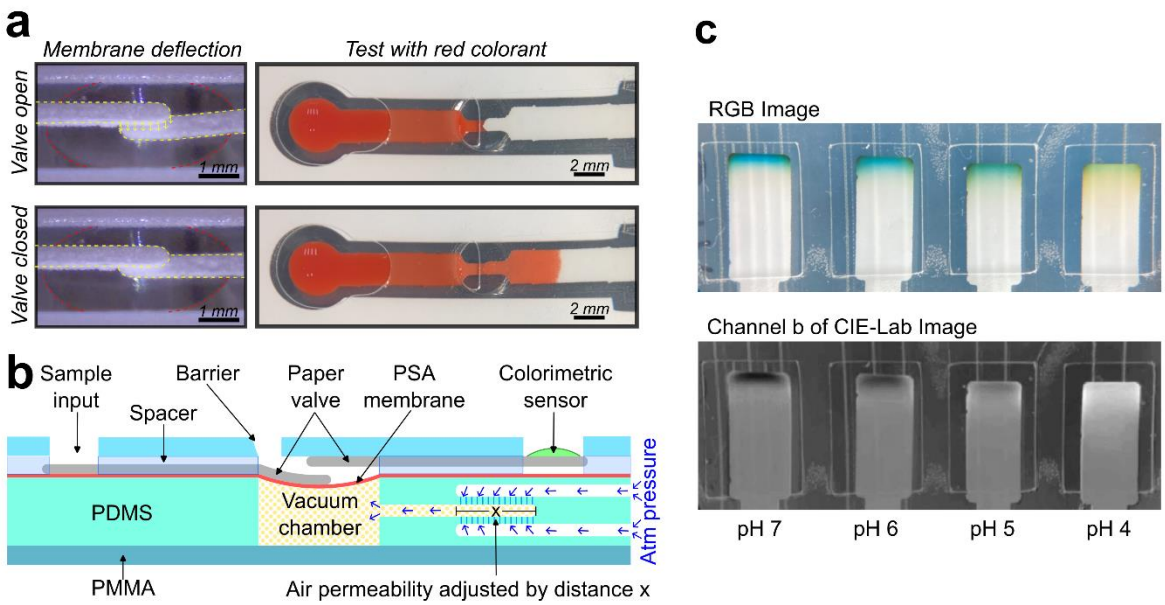


*Fig 1*. (**a**) Images showing the paper valve in its open or closed state and a test with red food dye. (**b**) Schematic of the flow path of the air through the PDMS. (**c**) Sensors of the paper valve device after reaction with four pH levels at different time points.

**Acknowledgments**

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