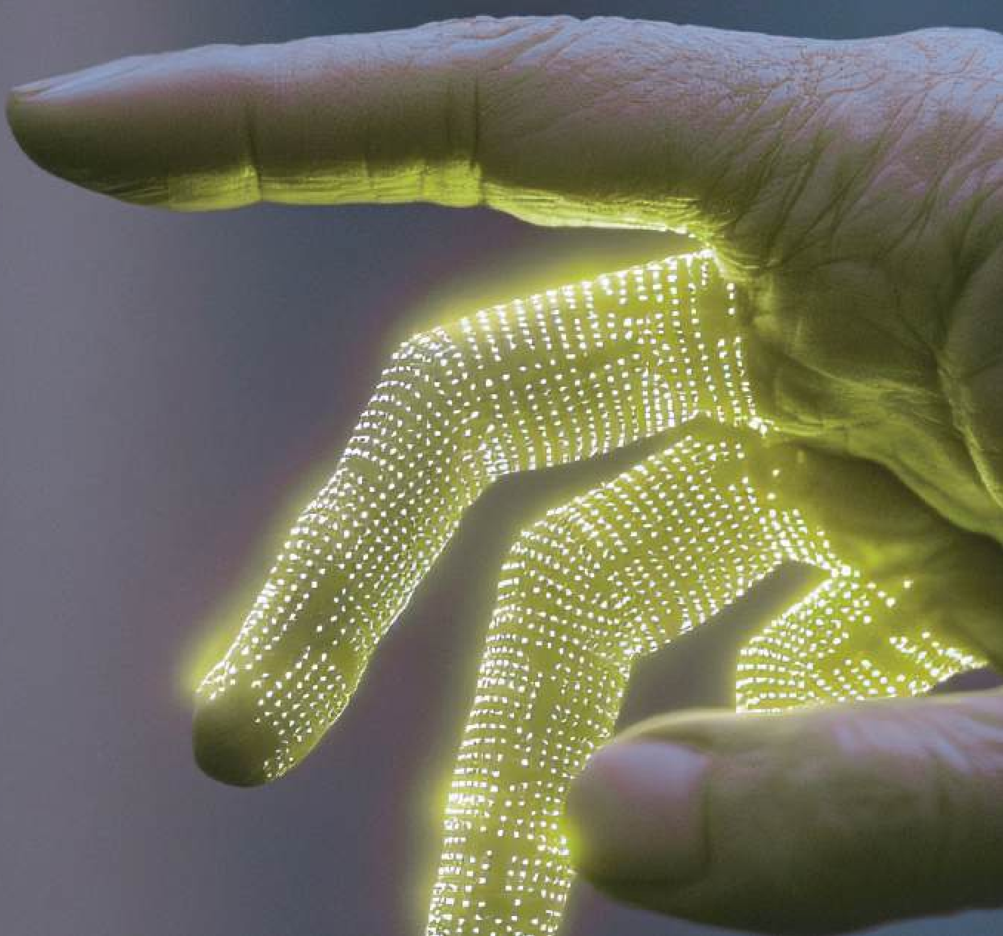
IBEC

Institute for Bioengineering of Catalonia

18th IBEC SYMPOSIUM

BIOENGINEERING

FOR PRECISION MEDICINE



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Welcome to IBEC's 18th annual Bioengineering for precision medicine

I am happy to meet you again in our annual symposium.

I hope that you'll be stimulated and inspired by our programme of talks, posters, and networking. This year we will have again a special poster session. Following your request, this year's poster session will be the day after the talks, giving you more time to raise questions and engage in deeper discussions about the excellent science carried out at IBEC.

Thank you very much for participating in the Symposium!

Josep Samitier

Director
Institute for Bioengineering of Catalonia (IBEC)

18th IBEC SYMPOSIUM
BIOENGINEERING
FOR PRECISION MEDICINE

Programme

Thursday 16th October

08:00 – 09:00	Registration
09:00 – 09:15	Opening ceremony
09:15 – 09:45	*Director's presentation* **Josep Samitier**, Director IBEC
09:45 – 10:20	**Melike Lakadamyali** · University of Pennsylvania Selected ICREA Professor 2025 Super-resolution imaging of chromatin structure in health disease
10:20 – 11:00	Flash presentations. Session 1
11:00 – 11:35	Coffee break
11:35 – 11:55	Alumni session: **Alejandro Torres-Sánchez** · EMBL Barcelona
11:55 – 12:30	**Evrim Acar Ataman** · Simula (Coupled) Tensor Factorizations – as a tool to develop knowledge-guided data-driven methods for extracting insights from complex data
12:30 – 13:15	Session on Translation
13:15 – 14:30	Lunch break
14:30 – 15:25	Flash presentations. Session 2
15:25 – 16:00	**Yuval Ebenstein** · Tel Aviv University Selected ICREA Professor 2025 From the Lab to the Clinic: A toolbox for epigenetic analysis of DNA

16:00 – 16:10	**Marc Riu** · PhD Committee
16:10 – 16:20	**Laasya Dhandapani** · Postdoc Committee
16:20 – 16:30	**Awards and closing ceremony** My Green Lab Certification Awards PhD Certificate of Excellence and Award Best Flash Talk

Friday 17th October

10:00 – 12:30	Poster Session


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Keynote Lectures

Super-resolution imaging of chromatin structure in health and disease

Lakadamyali, Melike

Super-resolution microscopy has opened new possibilities for visualizing chromatin architecture in situ at nanoscale resolution. Leveraging quantitative super-resolution imaging, we revealed the heterogeneous nature of nucleosome folding and demonstrated that chromatin structure at both nano- and meso-scales is highly plastic, dynamically remodeling in response to chemical and mechanical cues in health and disease. By combining biologically interpretable feature extraction with machine learning, we further showed that cells can be accurately classified into distinct states based solely on their multi-scale chromatin organization, while also identifying the specific chromatin features that drive classification, thus offering mechanistic insight into cell-state regulation.

Lakadamyali, Melike

Dr. Lakadamyali received exemplary training from Prof. Xiaowei Zhuang and Jeff Lichtman at Harvard University. In 2010 she joined the Institute of Photonic Sciences (ICFO) in Barcelona as an Assistant Professor and was promoted to Associate Professor with tenure in 2015. She relocated to the University of Pennsylvania, Perelman School of Medicine as an Assistant Professor in 2017, where she is now a Professor with tenure.

The overarching goal of the Lakadamyali lab is to understand the molecular mechanisms that regulate sub-cellular organization and the significance of this organization on cell function. Cells are highly compartmentalized: the sub-cellular positioning of organelles, nucleic acids and proteins are spatially and temporally coordinated to ensure that biochemical reactions take place at the right place and time. My program has three major focus areas that seek to advance our understanding of sub-cellular organization. In the context of the cytosol, I seek to determine how the microtubule cytoskeleton and motors regulate the transport and positioning of organelles within the cytoplasm and the functional consequences of disrupting proper organelle organization. In addition, I am interested in understanding how the molecular identity of organelles is linked to their spatial positioning and function. In the context of the nucleus, I seek to understand how the spatial organization of chromatin regulates gene activity in health and disease. To address these key biological questions, my lab takes an innovative approach of combining cell biological tools with advanced and highly quantitative microscopy tools including single-molecule tracking and super-resolution microscopy. My lab's work has been funded by the European Research Council (ERC-Starting grant), NIH and NSF.

Tuesday 16th October · 11:35 h

KEYNOTE LECTURE

Computational modelling: a toolbox to understand the mechanics of cells and tissues

Alejandro Torres

Computational modelling provides a powerful framework to explore how cells and tissues behave, interact, and respond to mechanical cues. By combining principles from biology and physics, models allow us to test hypotheses, interpret experimental data, and predict complex behaviours that are difficult to observe directly. In this talk, I will give an overview of how computational approaches can be used as a toolbox to study the mechanics of living systems, from the deformation of individual cells to the collective organisation of tissues. I will illustrate these ideas through two examples involving heart morphogenesis and malaria parasite cytoadhesion, the process by which infected red blood cells adhere to vessel walls.

Alejandro Torres

Alejandro Torres-Sánchez leads a research group at the European Molecular Biology Laboratory (EMBL) in Barcelona. He earned his PhD in Applied Mathematics from the Polytechnic University of Catalonia in 2017. Following postdoctoral work at the Francis Crick Institute and the Institute for Bioengineering of Catalonia, Alejandro established his own group at EMBL-Barcelona in 2022. His group integrates methods from theoretical physics and computational engineering to develop mathematical models and computer simulations to understand the behaviour of cells and tissues. In collaboration with experimentalists, his group applies these methods to understand the physical principles that underpin tissue self-organisation and shape generation.

Tuesday 16th October · 11:55 h

KEYNOTE LECTURE

(Coupled) Tensor Factorizations – as a tool to develop knowledge-guided data-driven methods for extracting insights from complex data

Evrim Acar

Datasets from diverse sources are collected in many applications to gain insights about complex systems such as the human brain and human metabolome, or to detect early risk factors for various diseases. For instance, joint analysis of omics data holds the promise to improve our understanding of the human metabolism and facilitate precision health. Such multimodal datasets are often noisy, incomplete, and multiway (i.e., with more than two axes of variation such as subjects, metabolites, and time). Some datasets change in time (e.g., longitudinal measurements) while some are static.

How can we jointly analyze such heterogeneous data and reveal interpretable patterns? How can we effectively incorporate prior information, e.g., the fundamental principles encapsulated in computational models, in real data analysis to reveal insights from such complex datasets?

Tensor factorizations have been successfully used to reveal the underlying patterns in multiway data in many domains, and have been extended to joint analysis of multimodal data through coupled tensor factorizations. Coupled tensor factorizations provide an explainable framework revealing interpretable patterns. In this talk, we will discuss (coupled) tensor factorization models and how to use them to extract interpretable patterns from complex datasets including temporal and multimodal datasets. We will also demonstrate how coupled tensor factorizations can be used to guide real data analysis with computational models. Throughout the talk, we will cover various applications, in particular, analysis of metabolomics measurements collected during a meal challenge test (e.g., to reveal evolving metabolite patterns, static and dynamic biomarkers of phenotypes, individual differences via subject-specific temporal trajectories), and analysis of neuroimaging signals (e.g., to reveal diagnostic biomarkers via multimodal neuroimaging data fusion, and to capture spatial brain dynamics).

Evrim Acar

Evrim Acar is a Chief Research Scientist at Simula Metropolitan Center for Digital Engineering (Oslo, Norway). She received the MS and PhD degrees in Computer Science from Rensselaer Polytechnic Institute (Troy, NY), and her BS degree in Computer Engineering from Bogazici University (Istanbul, Turkey). Her research focuses on data mining methods, in particular, tensor factorizations, multimodal data mining using coupled factorizations as well as their applications in diverse disciplines. Prior to joining Simula, Evrim was a faculty member at the University of Copenhagen (Denmark), and a postdoctoral researcher at Sandia National Labs (Livermore, CA). She is a recipient of the Sapere Aude Young Elite Researcher Award by the Danish Council for Independent Research. She is currently serving on the editorial board of SIAM Journal on Matrix Analysis and Applications (SIMAX). She has also held various positions in signal processing and data mining communities.

From the Lab to the Clinic: A toolbox for epigenetic analysis of DNA / Yuval Ebenstein

Yuval Ebenstein

DNA sequencing (NGS) is revolutionizing all fields of biological research. Still, it fails to extract the full range of information associated with genetic material and cannot resolve important variations between genomes. The information content of the genome extends beyond the base sequence in the form of chemical modifications such as DNA methylation or chromosomal association with DNA-binding proteins (chromatin). For the last decade, my lab has been developing tools for genomic analysis at the single-cell and single-molecule levels. I will show how the physical extension of long DNA molecules in nanofluidic channels reveals this information in the form of a linear, optical, or electrical “barcode,” like beads threaded on a string, where each bead represents a distinct type of observable. I’ll present a biochemical and physical toolbox for mapping epigenetic modifications in the genome and demonstrate its application in clinical cancer research. Finally, I will talk about a DNA chip developed in the lab and the adventure of building a startup based on this technology.

Yuval Ebenstein

Prof. Yuval Ebenstein is a scientist and entrepreneur with years of experience in translational research. Yuval is head of the NanoBioPhotonix Lab and the founder of the Tel Aviv University Entrepreneurship Center. In his lab, Yuval combines Chemistry, Physics, Biology, and bioinformatics in order to study the human genome. His lab explores genomes utilizing tools and reagents from the realm of nano-technology, zooming in on single cells, single chromosomes, and single molecules. Yuval is the winner of two ERC awards for developing genomic technologies and is the founder of JaxBio, a liquid biopsy methylation-based diagnostics startup.

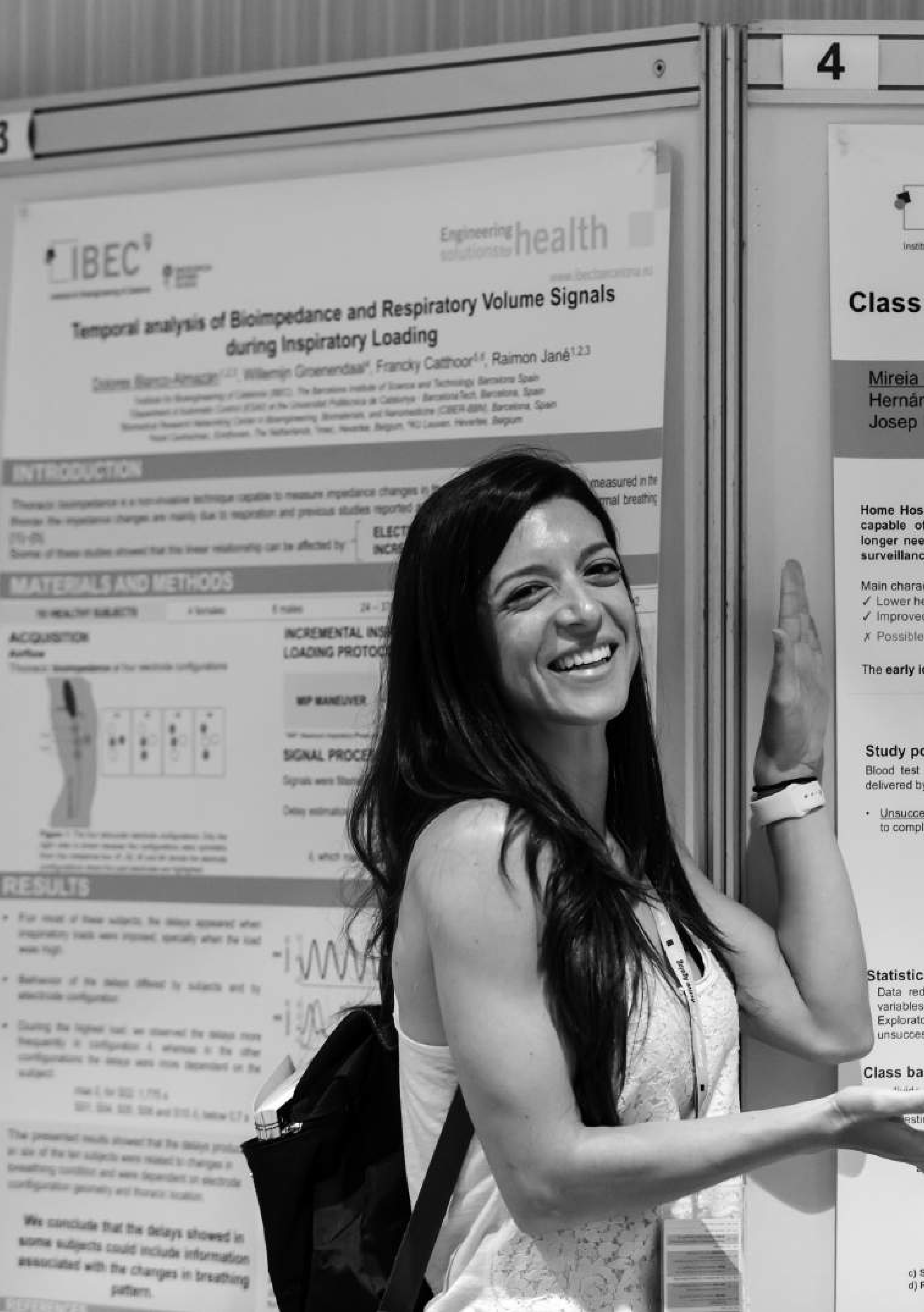
FLASH Presentations

FLASH PRESENTATIONS · SESSION 1

NAME	SURNAME	TITLE
Ainoa	Tejedera-Villafranca	Enhancing drug assessment for Duchenne muscular dystrophy using organ-on-a-chip technology and nanoplasmonic biosensing of myotube integrity
Anna	Vilche	Microphysiological Modeling of Human CNS Trauma and and Nanoparticle-Based Therapy Evaluation
Gal·la	Vinyes i Bassols	High-Throughput 3D Bioprinted Human Blood-Brain Barrier: Advancing *In Vitro* Modeling and Drug Screening for Neurodegenerative Diseases
Xiomara	Fernández Garibay	Calcitriol ameliorates myotonia in patient-derived DM1 skeletal muscle models via an MBNL1-independent mechanism
Peter	Sperling	13C NMR metabolomics to assess glucose metabolism in BxPC3 and HepG2 cell lines
Agnieszka	Nikitiuk	A ppreclinical platform for therapeutic testing: 3D tissue-engineered models of head and neck cancer
Júlia	Alcàcer Almansa	*Burkholderia cenocepacia* and *Pseudomonas aeruginosa* in dual-species models: Insights into population distribution, antibiotic susceptibility, and virulence

FLASH PRESENTATIONS · SESSION 2

NAME	SURNAME	TITLE
Marina	Placci	Nanomechanical traits for Rare Diseases: spotlight on Gaucher and Fabry diseases.
Thomas	Wilson	Engineering epithelial cell shape and mechanics to create a new generation of biohybrid devices
Juan Francisco	Abenza Martínez	The mechanical control of the mammalian circadian clock
Beatriz	Cantero Nieto	Highthroughput biomechanical characterization of macrophage polarization through atomic force microscopy
Kristin	Fichna	Nanomotor-Assisted intravesical chemotherapy for bladder tumor reduction and recurrence prevention
Marco	Basile	Modulating Blood-brain barrier low-density lipoprotein receptor-related proteins (LRP) receptors using multivalent drugs.
Tomás	Quiroga	Deep indel mutagenesis of the ALS protein SOD1 to comprehensively map the impact of mutations on protein abundance and dimer formation
Tiziana	Russo	A LEGO® like approach to i-combisomes origami
Claudia	Camarero	Disrupting protein aggregation as a novel strategy against malaria: mechanistic insights into YAT2150.
Carles	Prado Morales	Breaching the human skin barrier with degradable enzymatic nanobots
Mehdi	Torabi Goodarzi	VCSEL technology integration into plasmonic biosensors for miniaturized, low cost and portable systems



4
IBEC
Engineering solutions for health
Temporal analysis of Bioimpedance and Respiratory Volume Signals during Inspiratory Loading
Willemijn Groenendaal, Francky Catthoor, Raimon Jané
INTRODUCTION
MATERIALS AND METHODS
ACQUISITION
INCREMENTAL INS
LOADING PROTOC
MIP MANEUVER
SIGNAL PROCE
RESULTS
We conclude that the delays showed in some subjects could include information associated with the changes in breathing pattern.
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Imbalance Impact on the Prediction of Complications during Home Hospitalization: A Comparative Study

Calvo[1,2], Isaac Cano [4], Carme
ndez [4], Vicent Ribas [5], Felip Miralles [5],
Roca [4] Raimon Jané [1,2,3]

[1] *Biomedical signal processing and interpretation, Institute for Bioengineering of Catalonia (IBEC), Spain*
[2] *Barcelona Institute of Science and Technology (BIST), Spain*
[3] *Dept. of Automatic Control, Universitat Politècnica de Catalunya (UPC) – BarcelonaTech and Biomedical Research Networking Centre in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Spain*
[4] *Hospital Clínic de Barcelona, Spain*
[5] *Eurecat Technology Centre of Catalonia, Spain*

Introduction

pitalization (HH) is presented as a healthcare alternative f providing high standards of care when patients no d hospital facilities, but still require active and complex e [1].

cteristics of home hospitalization programs:
ealthcare-associated costs
d patient's quality of life
complications due to lack of continuous observation at home

dentification of patients who may not benefit from HH is key.

Blood tests have been proven to provide relevant prognosis information in many diseases [2].

- Hypothesis: patients not being eligible for HH programs could be identified through the construction of **predictive models** based on data from routine blood tests at the moment of admission.

Since conventional machine-learning methods are extremely sensitive to **class imbalance** and **unsuccessful HH cases** (eventually needing hospital facilities) are rare, they show a strong bias towards the majority class.

This study analyzes and compares several **sampling strategies** and their impact on classification performance, in this particular scenario.

Materials and methods

opulation

data (24 variables) from 1951 patients admitted to the HH program y Hospital Clinic de Barcelona (Spain), between 2012 and 2015.

essful group: 101 patients eventually needing regular hospitalization due ications of different origin.

	Successful (n=1850)	Unsuccessful (n=101)	p-value
Age, years old	70.6 ± 15.0	72.9 ± 14.3	0.072
Male sex, n (%)	1153 (62.3%)	66 (65.3%)	0.613
Main diagnosis, n (%)			
Cardiology	196 (10.6%)	26 (25.7%)	<0.001
Respiratory	573 (31.0%)	24 (23.8%)	0.156
Oncology	146 (7.9%)	8 (7.9%)	1.000
Surgery	366 (19.8%)	15 (14.9%)	0.236
Acute	569 (30.8%)	28 (27.7%)	0.594

Values are mean ± standard deviation or number of observations (%).

al analysis

undancy evaluation through **correlation analysis** between pairs of (*Spearman*).
ory analysis of **statistical differences** between successful and ssful cases for each variable (*Mann-Whitney U tests*).

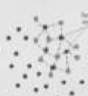
lancing

aining (75%) and testing (25%) subsets, using a stratified strategy.
model training were only applied to the first subset.
g subset was then used for classification performance quantification.

compares the following sampling techniques:

ng

b) Random over-sampling



ynthetic Minority Over-sampling TEchnique (SMOTE)
Random Over-Sampling Examples (ROSE)

Results

Correlation analysis

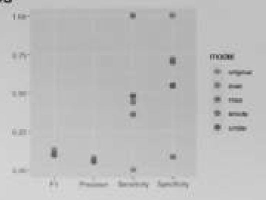
- **Hematocrit** was positively correlated with both **hemoglobin concentration** ($\rho = 0.98$) and **red blood cell count** ($\rho = 0.91$).
- Percentage and total amount of **neutrophils** ($\rho = -0.97$) and **lymphocytes** ($\rho = 0.96$) were highly correlated.

Statistical analysis

Statistically significant differences between successful and unsuccessful cases were observed for **lymphocytes percentage** ($p = 0.040$), **hemoglobin concentration** ($p = 0.030$), **total amount of lymphocytes** ($p = 0.023$), **creatinine** ($p = 0.023$) and **red cell distribution width** ($p = 0.002$).

Comparison of sampling approaches

- Original model heavily biased towards the majority class.
- All strategies showed low *Precision*:
  - Best *Sensitivity*: ROSE
  - Best F_1: Random over-sampling



Conclusions

I. Significant correlations were noted among variables. Thus, a **feature selection** step would be advisable to minimize data redundancy.
II. **Hemoglobin concentration**, **lymphocytes**, **red cell distribution width** and **creatinine** were found to unmask statistically significant differences between patients undergoing successful and unsuccessful HH stays.
III. Among the analyzed sampling approaches, over-sampling strategies, such as ROSE and random over-sampling, showed the best performances. Nevertheless, further improvements should be proposed in the future.

N	NAME	SURNAME	TITLE
1	Ainoa	Tejedera-Villafranca	Enhancing drug assessment for Duchenne muscular dystrophy using organ-on-a-chip technology and nanoplasmonic biosensing of myotube integrity
2	Anna	Vilche	Microphysiological Modeling of Human CNS Trauma and and Nanoparticle-Based Therapy Evaluation
3	Gal·la	Vinyes i Bassols	High-Throughput 3D Bioprinted Human Blood-Brain Barrier: Advancing *In Vitro* Modeling and Drug Screening for Neurodegenerative Diseases
4	Xiomara	Fernández Garibay	Calcitriol ameliorates myotonia in patient-derived DM1 skeletal muscle models via an MBNL1-independent mechanism
5	Peter	Sperling	13C NMR metabolomics to assess glucose metabolism in BxPC3 and HepG2 cell lines
6	Agnieszka	Nikitiuk	A ppreclinical platform for therapeutic testing: 3d tissue-engineered models of head and neck cancer
7	Júlia	Alcàcer Almansa	*Burkholderia cenocepacia* and *Pseudomonas aeruginosa* in dual-species models: Insights into population distribution, antibiotic susceptibility, and virulence
8	Marc	Palà	Engineering Ionic Combisomes through backbone molecular design
9	Marina	Rovira Mañe	Localised Electrical Stimulation of Engineered Skeletal Muscle Constructs Using rGO Microelectrodes
10	Florencia	Lezcano	Bioinspired bioprinting of skeletal muscle constructs with controlled fiber orientation
11	Armando	Cortés	Decoding skeletal muscle-liver axis in the context of sarcopenia: Towards the multi organ on a chip
12	Michela	Lain Contato	Evaluation of two targeted spatial proteomic platforms: CODEX and MIBI

N	NAME	SURNAME	TITLE
13	Natalia	Castro	Development of personalized bioinks for skeletal muscle tissue engineering to understand the role of the extracellular matrix in Duchenne muscular dystrophy
14	Adriana	Lattanzi	Comparative deep mutagenesis of CAPRIN1 to uncover the mechanism by which its pathogenic variant P512L causes neurodevelopmental disorders
15	Jaime	Casado	In Situ Tracking of Clonal Evolution and Phenotypic Heterogeneity in Tumors by Spatial Epitope Barcoding
16	Carles	Verdaguer	Developing an *in vitro* 3D model to track tumor-macrophage interactions with spatial proteomics
17	Aleixandre	Rodrigo Navarro	Optogenetic gene expression control in *Lactococcus lactis*
18	Júlia	Fabà Costa	An ex utero embryo culture platform to address peri-implantation development
19	Victoria	Batto	Immunosuppressive microenvironment shaped by collagen dynamics in lung adenocarcinoma
20	Anisha	Pahuja	Exploiting human pluripotent stem cells to study human disease in kidney and retina.
21	Vladislav	Petrovskii	Ordering competition drives tunable properties in cell-mimicking membranes
22	Karolina	Zimkowska	AAV-Driven P301L-Tau Expression Modulates Neuronal Activity in Human Cortical Brain Organoids
23	Inés	Martínez	Role of GPR133 in Modulating Neuronal Susceptibility and Synaptic Plasticity: Insights from a Knockout Mouse Model
24	Luciano	Riso	Tuning cryogel pore orientation for mimicking cartilage architecture
25	Nuria	Moral	Uncovering the Role of Glycogen in GABAergic Interneurons in Lafora Disease-Associated Epilepsy

N	NAME	SURNAME	TITLE
26	Yunuen	Avalos Padilla	Disruption of proteostasis and growth impairment in *Plasmodium falciparum* by an Intrinsically disordered PfUT segment
27	Lluis	Mangas Florencio	Parallel Cellular Metabolic Imaging by Merging MRI and Microfluidics for Personalised Medicine
28	Francisco Manuel	Sáez González	Humanized Models for Studying Spinal Cord Injury and Developing Therapeutic Strategies
29	Dayaneth	Jácome	3D Glioblastoma Spheroid Model for Natural Hypoxia Induction to Investigate microRNA-Based Therapeutic Strategies Targeting PrPC Overexpression
30	Joel	Àlvarez Puig	Studying the interactions of prosthetic joint infection associated pathogens in a *Galleria mellonella* infection model
31	Palash	Chandravanshi	Engineering ECM-Mimetic Platforms for Functional Maturation of iPSC-Derived Motor Neurons in 3D Printed Spinal Cord Constructs
32	Chiara	Ninfali	Modeling fibrosis and muscle function in Duchenne Muscular Dystrophy (DMD) using an engineered 3D Co-Culture system.
33	Eduard	Torrents	FleQ-Dependent Regulation of the Ribonucleotide Reductase Repressor nrdR in *Pseudomonas aeruginosa* During Biofilm Growth and Infection
34	David	Bartolomé Català	Advanced *in vitro* models show tumor modulation of T cell migration in colorectal cancer microenvironments
35	SERAFIMA	BELETSKAYA	Identifying the Key Factors of Matrisome Remodeling for Spinal Cord Injury Treatment

N	NAME	SURNAME	TITLE
36	Mehdi	Torabi Goodarzi	VCSEL technology integration into plasmonic biosensors for miniaturized, low cost and portable systems
37	David Esteban	Suárez Baquero	2P-FENDO: A Flexible Fiberscope for Investigating Inter-regional Brain Circuits in Freely Behaving Animals
38	Yoel	Melul	A Closed-Loop System for Real-Time Calcium Imaging, Neuron Selection, and Targeted Photostimulation in Freely Moving Mice
39	Hamed	Karami	Smart Sensing and Signal Processing Techniques for Early Detection of Oxidation in Extra Virgin Olive Oil
40	Hamed	Karami	Rapid Assessment of Coffee Aroma Profiles Using Multi-Sensor Arrays and Supervised Learning Models
41	Mohamed Aziz	Ouhida Ben Romdhane	Wasserstein GAN-Based Data Augmentation for Urine GC-IMS Chromatograms
42	Tecla	Duran	Removing Systematic Variability from GC-IMS Measurements with Orthogonal Projections
43	Elena	Sossich	Peptide-Based Biosensor for Early Detection of Multiple Sclerosis via Activated VLA-4$^+$ Cells
44	Gergo	Matajsz	13C metabolic imaging methods development for chorioallantoic membrane (CAM) assays
45	David	Gomez-Cabeza	A probabilistic study to uncover biological systems' properties via hyperpolarised nuclear magnetic resonance
46	Martín	Ruiz Gutiérrez	Surface plasmon resonance sensing platform for real-time fibrosis monitoring of Duchenne Muscular Dystrophy organ-on-a-chip model

N	NAME	SURNAME	TITLE
47	Petra	Bauzon	Biosensing in complex media: development of an anti-fouling biofunctionalization strategy for plasmonic biosensors.
48	Daniel	Romero	Feasibility of cellulose-based electrodes for ECG parameter analysis: preliminary assessment in healthy volunteers
49	Manuel	Lozano	Performance Evaluation of Tattoo Skin Electrodes for Measuring Respiratory Muscle Activity in Healthy Subjects
50	Yolanda	Castillo	Assessment of Sleep Apnea in Stroke Patients using Smartphone Technology

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51	Thomas	Wilson	Engineering epithelial cell shape and mechanics to create a new generation of biohybrid devices
52	Juan Francisco	Abenza Martínez	The mechanical control of the mammalian circadian clock
53	Marina	Placci	Nanomechanical traits for Rare Diseases: spotlight on Gaucher and Fabry diseases.
54	Beatriz	Cantero Nieto	Highthroughput biomechanical characterization of macrophage polarization through atomic force microscopy
55	Mauricio	Cano Galván	Mechanotool: Towards an Autonomous Open-Source Software Platform for Large-Scale Mechanical Analysis of Bio-Atomic Force Microscopy data
56	Yogita	Maithani	Local conduction properties of cable bacteria fiber sheaths after UV and humidity exposure using scanning dielectric force microscopy
57	Rohit	Nautiyal	Role of nematic order in tissue reshaping
58	Janet	van der Graaf Mas	Experimental model of the mechanobiology of the immunocompetent tumor ecosystem
59	Alice	Perucca	Fibroblast nematicity as a tool to study stromal control on immune migration.
60	Mireia	Valero Puigdomenech	Macrophage polarization in viscoelastic environments
61	Margherita	Gallano	Nuclear Envelope Remodeling and Mechanosensing Mechanisms under Stretch
62	Jorge	Oliver-De La Cruz	Stiffness-Regulated Microtubule Stability Controls Tau Phosphorylation and Nuclear Localization in Neurons
63	Guillermo	Martínez Ara	An optogenetic toolset to understand and control epithelial mechanical balance
64	Aurora	Dols Perez	Nanomechanics of long-distance electron conductive multicellular cable bacteria

N	NAME	SURNAME	TITLE
65	valeria	venturini	Force transmission and mechano-transduction from cell-cell adhesions to the nucleus
66	Gotthold	Fläschner	Nuclear mechanics regulates the organization of FG-nups in nuclear pore complexes
67	Marc	Rico Pastó	Shear stress resistance reveals metastatic potential in solid tumor cell lines
68	Aina	Albajar Sigalés	Studying the mechanical regulation of nucleocytoplasmic transport using Single Molecule Tracking
69	Mariana	Azevedo Gonzalez Oliva	Piezo1 regulates the mechanotransduction of soft matrix viscoelasticity
70	Pol	Picón Pagès	Mechanistic Insights into GPR133 Signaling in Glioblastoma Multiforme
71	Ona	Baguer Colomer	Role of nuclear mechanics in the regulation of EMT in pancreatic cancer cells
72	Carolina	Rodríguez-Gallo	Magnetic actuators: Inducing stretching in functional 3D muscle human engineered models
73	Miguel	González Martín	Designing mechanosensible molecules for the mechanical control of cellular transcription
74	Montserrat	Sales Mateo	Electrochemical Tunneling Spectroscopy Study of Charge Transport in the Redox Protein Plastocyanin, its pH Dependence, and Copper Ion Role
75	Steffen	Grosser	Mechanical polarity in cell migration
76	Jordi	Comelles	Long-range organization of primary intestinal fibroblasts guides directed and persistent migration of organoid-derived intestinal epithelia
77	Amélie	Godeau	Two phases of invasion associated to trophoblast differentiation in autonomous human embryo implantation
78	Clément	Hallopeau	Mechanical confinement controls stemness and cell flows in the intestinal crypt

N	NAME	SURNAME	TITLE
79	Kristin	Fichna	Nanomotor-Assisted intravesical chemotherapy for bladder tumor reduction and recurrence prevention
80	Marco	Basile	Modulating Blood-brain barrier low-density lipoprotein receptor-related proteins (LRP) receptors using multivalent drugs.
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83	Claudia	Camarero	Disrupting protein aggregation as a novel strategy against malaria: mechanistic insights into YAT2150.
84	Carles	Prado Morales	Breaching the human skin barrier with degradable enzymatic nanobots
85	Jordi	Alcalà Barrat	Effect of UV Irradiation and Humidity on the Electrical Conductivity of Cable Bacteria Sheaths
86	David	Esporrín Ubieto	Enzymatic nanomotors based on chemically-crosslinked nanogels with enhanced motion in viscous media for biomedical applications
87	Valentino	Barbieri	Harnessing Structural Complexity for Phenotypic Targeting
88	Inés	Macías Tarrío	Biocompatible nanobots for personalized bladder cancer therapy: mechanisms of action and therapeutic efficacy
89	Giulia	Porro	Studying LRP1 endocytosis and recycling kinetics at the BBB in Alzheimer's disease
90	Ainhoa	González Caelles	Engineered PLGA Nanobots for RNAi-Based Treatment of Bladder Cancer
91	Dario	Castellana	Radioprotection and Tissue Regeneration in resectable Head and Neck Squamous Cell Carcinoma

N	NAME	SURNAME	TITLE
92	Albert	Ripoll	Colistin-loaded nanoparticles in combination with alginate lyases enhance *Pseudomonas aeruginosa*'s biofilm disruption
93	Núria	Blanco-Cabra	*Galleria mellonella* as a simple yet reliable *in vivo* model for nanotoxicology
94	Elena	Muscolino	Nanomedicine for the treatment of Lafora disease: use of mRNA-loaded polymeric nanoparticles as an innovative replacement therapy
95	Roger	Fàbrega Alsina	The Physicochemical, biopharmaceutical, and *in vitro* efficacy properties of diclofenac-loaded liposomes
96	Silvia	Muro	Identification of an anti-ICAM-1 antibody for improved isoform-dependent targeting and transport across the blood-brain barrier
97	Ángela	Martínez Mateos	DnaA acts as a transcriptional activator that regulates nrdAB ribonucleotide reductase expression in *Pseudomonas aeruginosa* PAO1
98	Carla	Arroyo	Tiny Signals, Big Impact: Toward Personalized Monitoring of Cardiovascular Health
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N	NAME	SURNAME	TITLE
100	Gender	Comission	Promoting Gender Equality, Diversity, and Inclusion at IBEC: Goals and Actions of the Gender and Diversity Commission

FLASH PRESENTATION | CELL ENGINEERING

FLASH 1 presented by:

NAME: Ainoa Tejedera-Villafranca

Enhancing drug assessment for Duchenne muscular dystrophy using organ-on-a-chip technology and nanoplasmonic biosensing of myotube integrity

Ainoa Tejedera-Villafranca[1], Martín Ruiz-Gutiérrez, Mehdi Torabi[1], María J Ugarte-Orozco[1], Armando Cortés-Reséndiz[1], Javier Ramón-Azcón[1,2], and Juan M. Fernández-Costa

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Duchenne muscular dystrophy (DMD) poses significant challenges for drug development, given its complex and degenerative pathology. While extensive research has explored potential treatment molecules, the success rate remains limited, partially due to the limitations of standard preclinical research tools. To accelerate the evaluation of anti-DMD treatment candidates, we introduce an innovative Organ-on-a-Chip (OOC) platform.

This technology offers a novel and promising approach to DMD drug development. The OOC platform comprises a microfluidic device capable of sustaining the culture and electrical stimulation of six patient-derived 3D contractile skeletal muscle tissues. The device is interconnected to a nanoplasmonic sensing device that enables the individual monitoring of myotube integrity for each muscle tissue as a key indicator of anti-DMD drug efficacy. The DMD *in vitro* model is constructed by encapsulating myogenic precursors in a fibrin-composite matrix using a PDMS casting mold. Following a regimen of electrical pulse stimulation based on continuous contractile stimuli, our model faithfully recapitulates the membrane fragility observed in DMD, as evidenced by reduced myotube integrity and elevated Creatine Kinase (CK) levels in the culture medium.

The nanoplasmonic biosensor is integrated, offering fast, direct, and labelfree measurement of CK levels, thereby enhancing the assessment of sarcolemmal damage. This technology takes advantage of surface plasmon resonance phenomena to detect biomarkers in the order of picograms, and its integration with the microfluidic device allows an independent, online monitoring of myotube integrity after electrical stimulation and drug administration. Following this approach, we used this OOC platform to assess the ability of drug candidates for DMD to reduce membrane fragility, such as utrophin upregulators. This innovative fusion of OOC and plasmonic sensing technologies represents a transformative approach to DMD drug evaluation. By combining microfluidics, contractile 3D muscle models, and nanoplasmonic CK monitoring, our platform provides a powerful tool for assessing the efficacy of anti-DMD treatments. This work underscores the potential of OOC technology in advancing the development of therapies not only for DMD but also for other neuromuscular disorders.

FLASH 2 presented by:

NAME: Anna Vilche

Microphysiological Modeling of Human CNS Trauma and Nanoparticle-Based Therapy Evaluation

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Traumatic injuries affecting the central nervous system (CNS)—including both brain and spinal cord—present major clinical challenges due to their complex and severity-dependent pathophysiology. Conventional animal models often fall short in accurately reflecting human responses, underscoring the need for advanced physiologically relevant *in vitro* systems. In this study, we introduce a novel human-based microphysiological platform engineered to model CNS trauma, specifically contusive traumatic injury (TI), using a polydimethylsiloxane (PDMS)-based device. The system features a central chamber where a controlled mechanical impact recapitulates the biomechanics of CNS contusion. It supports a mixed neural co-culture that replicates the cellular heterogeneity of brain tissue, enabling detailed investigations into injury progression and therapeutic efficacy.

To explore neuroregenerative strategies, we employed biodegradable polymeric nanoparticles (NPs) made from PLGA, functionalized with two targeting peptides: pVEC, to enhance penetration across cellular barriers, and NCAM for selective neuronal targeting. These NPs were further surface-modified with polyethylene glycol (PEG) to increase stability and prolong systemic circulation and were loaded with riluzole—a neuroprotective compound previously tested in both preclinical and clinical models of CNS trauma [1,2].

Our findings reveal that microglial activation plays a key role in glial scar formation through the release of pro-inflammatory cytokines, exacerbating secondary injury. Administration of riluzole-loaded NPs markedly enhanced neuronal survival, stimulated neurite extension, and reduced glial scarring *in vitro*— demonstrating greater efficacy than free riluzole. These *in vitro* results were validated *in vivo* using a murine model of spinal cord compression, where treatment with riluzole-NPs resulted in significantly improved motor function recovery compared to controls.

Taken together, this work presents a reproducible and human-relevant *in vitro* model for studying CNS trauma, along with a promising therapeutic approach based on targeted nanoparticle delivery. The platform serves as an effective translational bridge between *in vitro* screening and *in vivo* validation, offering a tool to accelerate the development of clinically viable treatments for CNS injuries.

FLASH PRESENTATION | CELL ENGINEERING

FLASH 3 presented by:

NAME: Gal·la Vinyes i Bassols

High-Throughput 3D Bioprinted Human Blood-Brain Barrier: Advancing *In Vitro* Modeling and Drug Screening for Neurodegenerative Diseases

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The highly selective permeability of the blood-brain barrier (BBB) is crucial for protecting the brain from toxic substances, yet it simultaneoulsy poses a substantial obstacle to central nervous system (CNS) drug delivery, severely limiting the effectiveness of therapies targeting the brain. This challenge is reflected in the clinical landscape, where nearly 80% of drug candidates for neurodegenerative diseases (NDDs) fail in trials, resulting in the lowest approval rate among all therapeutic areas. To address the pressing need for more predictive and physiologically relevant NDD models, we introduce a three-dimensional (3D) bioprinted human BBB platform that versatility recapitulates both physiological and pathological CNS conditions *in vitro*. Leveraging a novel, microvalve-based embedded 3D bioprinting approach, our automated system enables high-throughput fabrication and precise spatial placement of cells with excellent viability. Using a low-viscosity bioink composed of fibrinogen, alginate, and brain microvascular endothelial cells (BMECs), we reproducibly generate ring-patterned scaffolds—up to 48 constructs in just 9 minutes—by droplet deposition into a crosslinking bath. After alginate removal, BMECs proliferate and self-organize within the fibrin matrix, forming intricate, branching vascular networks within a week. This versatile platform also supports the integration of additional neural cell types, enabling comprehensive studies of neurovascular interactions and the dynamic crosstalk between neural and vascular compartments. Furthermore, the system allows for the targeted introduction of drugs, nanoparticles, or neuroimaging agents into the luminal compartment, facilitating a wide range of applicavasctions including investigations of brain physiology, disease mechanisms, drug efficacy and safety, and neuroimaging probe development. Collectively, our findings establish a robust, scalable, and cost-effective 3D bioprinted BBB model that offers significant potential to bridge the gap between preclinical research and clinical translation in neurodegenerative disease drug development.

CELL ENGINEERING FLASH PRESENTATION

FLASH 4 presented by:

NAME: Xiomara Fernández Garibay

Calcitriol ameliorates myotonia in patient-derived DM1 skeletal muscle models via an MBNL1-independent mechanism

Xiomara Fernández-Garibay [1], Maria Sabater-Arcís [2,3], Ainoa Tejedera-Villafranca [1], Judit Núñez-Manchón [4], Rubén Artero [2,3], Mònica Suelves [4], Gisela Nogales-Gadea 4, Javier Ramón-Azcón [1,5], Juan M. Fernández-Costa [1]

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Myotonic Dystrophy Type 1 (DM1) is a severe, multisystemic genetic disorder characterized by progressive muscle weakness, atrophy, and myotonia. While traditional 2D culture systems and animal models have advanced our understanding of DM1 molecular pathways, they fall short of replicating the contractile and heterogeneous nature of the disease. To overcome these limitations, we engineered contractile 3D human skeletal muscle tissues using immortalized myoblasts from three DM1 patient-derived lines representing juvenile, adult, and late-onset subtypes. These cells were embedded in biocompatible hydrogel scaffolds and anchored between flexible posts to support alignment, maturation, and spontaneous contraction. The resulting tissues faithfully modeled key DM1 features, including MBNL1 sequestration in ribonuclear foci and widespread splicing defects. Notably, for the first time *in vitro*, we detected mis-splicing of CLCN1, the chloride channel associated with myotonia. Our model also recapitulated patient-specific functional phenotypes, such as muscle weakness, fatigue, and myotonia — previously observed only *in vivo*.

Pharmacological treatment with small molecules that increase MBNL1 levels partially rescued molecular and functional defects. Among them, Calcitriol significantly reduced myotonia without restoring MBNL1 distribution or CLCN1 splicing, indicating a novel MBNL1-independent mechanism. Transcriptomic analysis (RNA-seq) revealed that Calcitriol restores gene expression profiles altered in DM1, upregulating genes involved in neuromuscular transmission, metabolism, and synaptic signaling that are downregulated in DM1, and downregulating genes associated with stress, inflammation, fibrosis, and dysregulated development, which are upregulated in our DM1 models. This bidirectional gene expression correction aligns with the observed functional improvements.

Altogether, our 3D DM1 muscle model represents a highly relevant, patient-specific platform for therapeutic testing. It enables the study of contractile phenotypes and identifies Calcitriol as a promising modulator of DM1 pathology through an MBNL1-independent transcriptional mechanism.

FLASH PRESENTATION | CELL ENGINEERING

FLASH 5 presented by:

NAME: Peter Sperling

13C NMR metabolomics to assess glucose metabolism in BxPC3 and HepG2 cell lines

Peter Christian Sperling and Lluïsa Mora Rentero
IBEC

Pancreatic and liver cancers are among the deadliest conditions globally, projected to cause over 1.3 million deaths by 2025[1,2]. These diseases not only threaten patient survival but also place a heavy burden on global healthcare systems.

A defining feature of many cancers is the Warburg effect. This refers to a metabolic shift where cancer cells rely heavily on glycolysis for energy, even when oxygen is present.

Targeting this glycolysis-dominant metabolism is gaining clinical relevance. In pancreatic cancer, elevated glycolytic activity correlates with poor prognosis and disease progression. Inhibition using 2-deoxy-D-glucose (2-DG) reduces cell viability, suggesting that metabolic intervention may improve outcomes[3].

To investigate this vulnerability, we developed a ^{13}C NMR-based metabolomics protocol to characterize glucose metabolism in HepG2 (liver) and BxPC3 (pancreatic) cancer cell lines. This method aims to identify metabolic biomarkers and evaluate glycolytic inhibition as a precision medicine approach.

Cells were cultured in glucose-free EMEM (HepG2) or RPMI (BxPC3) supplemented with 10% FBS and 25 mM [U-$^{13}C_6$] glucose. After 3 h incubation, cells were washed with PBS, trypsinised, pooled, and counted. Pellets (10–30 million cells) were snap-frozen. Metabolites were extracted using cold 80% methanol-d_4/20% D_2O and analyzed by ^{13}C NMR to assess glucose incorporation.

Preliminary results revealed distinct labeling patterns. BxPC3 cells showed elevated lactate production, consistent with enhanced glycolytic flux. HepG2 cells displayed broader ^{13}C label distribution, suggesting partial reliance on oxidative pathways[4]. Treatment with glycolytic inhibitors reduced cell viability in both lines, with BxPC3 showing greater sensitivity, highlighting its metabolic vulnerability.

These findings provide a foundation for understanding cancer-specific glucose metabolism using ^{13}C NMR. The distinct glucose utilization profiles in HepG2 and BxPC3 support the therapeutic potential of glycolysis-targeted interventions, especially in pancreatic cancer. Future work will combine these data with hyperpolarized magnetic resonance to gain deeper insight into dynamic metabolic reprogramming.

1. https://doi.org/10.1016/j.jhep.2022.08.021

2. https://doi.org/10.3390/cancers17101607

3. https://doi.org/10.1016/j.biopha.2019.109521

4. https://doi.org/10.1007/s10863-015-9628-6

FLASH 6 presented by:

NAME: Agnieszka Nikitiuk

A ppreclinical platform for therapeutic testing: 3D tissue-engineered models of head and neck cancer

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Head and neck cancer squamous cell carcinoma (HNSCC) is the sixth most common cancer globally, with poor prognosis driven by high heterogeneity, drug resistance, and frequent metastasis. Human papilloma virus (HPV) status is a key determinant of tumor biology and therapeutic response, yet current preclinical models fail to recapitulate the tumor microenvironment (TME) and its impact on treatment efficacy. To address this gap, we developed a stratified 3D *in vitro* HNSCC model that mimics critical features of the TME. Multicellular spheroids were generated from of HPV-negative (Cal27) and HPV-positive (SCC152) HNSCC cell lines, co-cultured with human microvascular endothelial cells (HMEC-1) and human dermal fibroblasts (HDF). These spheroids were embedded in biologically relevant extracellular matrix (ECM hydrogels composed of collagen, fibrin, or collagen enriched with cell-derived matrix (CDM) from human adipose-derived mesenchymal stem cells (hAMSCs). An alternative model included fibroblast cells dispersed within the embedding matrix to simulate stromal architecture.

Morphological analysis revealed key differences between HPV+ and HPV– spheroids and the impact of culture conditions. SCC152 (HPV+) spheroids were bigger, more compact, and cohesive than CAL27 (HPV–), with tri-culture conditions (fibroblast inclusion) reducing spheroid diameter and altering morphology. These changes suggest fibroblast-mediated matrix remodelling and paracrine signalling may restrict spheroid expansion, mimicking *in vivo* desmoplasia. By Day 4, CAL27 spheroids in collagen exhibited radial spreading and flattening, likely promoting matrix invasion and increasing drug permeability due to enhanced cell–matrix adhesion. Drug testing with cisplatin and doxorubicin demonstrated matrix- and cell composition–dependent chemoresistance. Notably, tri-culture spheroids embedded in collagen matrices exhibited the highest drug resistance, with IC_{50} values up to 100-fold higher than spheroids cultured in medium alone. HPV-positive spheroids consistently showed enhanced resistance, likely due to compact morphology and inherent molecular mechanisms.

In conclusion, we established a physiologically relevant HPV-stratified 3D HNSCC platform with translational potential for preclinical drug screening and precision medicine applications. This model offers a promising tool to bridge the gap between conventional *in vitro* systems and clinical response, particularly in the context of non-animal, mechanism- informed therapeutic testing.

FLASH PRESENTATION | CELL ENGINEERING

FLASH 7 presented by:

NAME: Júlia Alcàcer Almansa

Burkholderia cenocepacia and *Pseudomonas aeruginosa* in dual-species models: Insights into population distribution, antibiotic susceptibility, and virulence

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Multispecies biofilms are communities composed of different microorganisms embedded in an auto-synthesized polymeric matrix. *Pseudomonas aeruginosa* and *Burkholderia cenocepacia* are two multidrug-resistant and biofilm-forming opportunistic pathogens often found in the lungs of people living with cystic fibrosis. In this context, planktonic, static, and dynamic biofilms and *in vivo* models of both species were optimized in this work to understand their population dynamics, disposition, virulence, and antibiotic susceptibility. From the coculture models optimized in this work, we determined that *B. cenocepacia* grows in a clustered, aggregative manner at the bottom layers of biofilms, in close contact with *P. aeruginosa*, that tends to occupy the top layers. Their coexistence increases virulence-related gene expression in both species at early stages of coinfection and in *in vivo* models, while there was a general downregulation of virulence-related genes after longer coexistence periods as they eventually reach a non-competitive stage during chronic infections. When evaluating antimicrobial susceptibility, a decrease of antimicrobial tolerance was observed in both species when co-cultured.

These findings shed light on the differential behavior of *P. aeruginosa* and *B. cenocepacia* in dual-species systems, stressing the relevance of multispecies studies in the clinical context.

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Alcàcer-Almansa, J., Blanco-Cabra, N., Torrents, E. (2025). Burkholderia cenocepacia and Pseudomonas aeruginosa in dual-species models: Insights into population distribution, antibiotic susceptibility and virulence. Virulence. 16(1): 2494039. https://doi.org/10.1080/21505594.2025.2494039.

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POSTER 8 presented by:

NAME: Marc Palà

Engineering Ionic Combisomes through backbone molecular design

Palà, Marc [1], Quandt, Jonas [3,4], Wagner, Anna M. [3,4], Russo, Tiziana [1,2], Englert, Jenny [3,4], Petrovskii, Vladislav S. [1], Kostina, Nina Yu. [1], Rodriguez-Emmenegger, César [1,3,5,6]

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Vesicles are central to synthetic cell design, providing membrane platforms where structure, mobility, and functionality must be precisely engineered to mimic biological systems. Ionic combisomes (i-combisomes) are a novel class of artificial vesicles formed from amphiphilic ionic comb polymers (iCPs). Their unique architecture act as hybrid between liposomes and polymersomes, exhibiting biomimetic membrane thickness, high thermal stability (up to 80 ºC), exceptional lateral membrane mobility, and high potential for functionalization. To advance the development of these novel vesicular platforms, a deeper understanding of how molecular design parameters influence i-combisome structure and behaviour is essential. In this study, we explored how backbone rigidity and intra-/inter-molecular hydrogen bonding modulate the self-assembly of iCPs into i-combisomes. We prepared a library of combs consisting of (meth)acrylate and (meth)acrylamide carboxybetaines and dimethylaminopropyl monomers by aqueous single electron transfer living radical polymerization (SET-LRP). Backbones were then complexed with lipid-like didodecyl phosphate (DDP) to afford the amphiphilic iCPs. Using a combination of polymer synthesis, self-assembly approaches, and the integration of high-resolution microscopy with molecular simulations, we aim to elucidate how backbone chemistry dictates i-combisome behaviour in aqueous environments. This approach is expected to identify design principles for engineering biomimetic vesicles, offering new directions for the development of functional synthetic cell membranes and polymer-based bioinspired systems.

POSTER CELL ENGINEERING

POSTER 9 presented by:

NAME: Marina Rovira Mañe

Localised Electrical Stimulation of Engineered Skeletal Muscle Constructs Using rGO Microelectrodes

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Tissue-engineered skeletal muscle models have been successfully developed to actuate biohybrid machines. Electrical stimulation of these actuators is applied to induce controlled movement. Usually, this is achieved by using conventional electrodes directly immersed in the culture medium, stimulating the whole tissue at once. Effective and selective actuation of these tissues is fundamental to the correct functionality of the biohybrid machines [1]. However, controlled localized stimulation of specific tissue areas has not been reported in the literature. The aim of this study is to locally stimulate these skeletal muscle actuators with reduced graphene oxide (rGO) based microelectrodes. With this purpose, C2C12-based skeletal muscle rings were fabricated by the mold casting method and matured for 14 days. The rings were then electrically stimulated using rGO microelectrodes for 15, 30 and 60 minutes. Contractile force was assessed by measuring the bending of cylindrical PDMS pillars [2]. An immunostaining of the rings was performed to evaluate any change in the fiber alignment and integrity. Finally, gene expression analysis was also conducted to assess molecular responses to stimulation. Localised contraction was successfully induced using rGO microelectrodes; with contractile force increasing across all stimulation periods. After 60 minutes of stimulation, myotube alignment was preserved, although signs of structural disruption were observed. These findings demonstrate that rGO microelectrodes can be effectively used to induce controlled stimulation in engineered muscle constructs, offering new opportunities for the precise control of bioactuator systems.

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POSTER 10 presented by:

NAME: Florencia Lezcano

Bioinspired bioprinting of skeletal muscle constructs with controlled fiber orientation

Lezcano, Florencia [1]; Fuentes, Judith [1]; Rovira, Marina [1]; Álvarez, Serxio [1]; Sánchez, Samuel [1,2]
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3D bioprinting allows the precise arrangement of cells, materials and functional molecules at the desired place in a pre-designed structure, enabling the construction of reproducible and scalable tissues which could be capable of imitate the complexity of natural tissue. However, skeletal muscle construct designs in literature are largely limited to simple shapes such as sheets, layered structures, lattices, grids, and circular or polygonal rings. Despite advancements in bioinks, printing approaches, and established techniques, achieving complex shapes with desired fiber orientation remains challenging. We hypothesized that by precisely controlling the 3D printing process and using dedicated anchor systems to support and guide fiber maturation, complex muscle designs with controlled shape and fiber arrangement could be achieved. Therefore, this study aimed to obtain bioprinted skeletal muscle constructs inspired by the natural shape and fiber disposition of human muscles. For this purpose, skeletal muscle constructs with parallel, fusiform, bipennate, and circular shapes were 3D printed using an extrusion printer controlled by a custom-made, high-precision, Python-based tool. First, a dedicated PDMS anchor system was 3D printed on a petri dish and cured overnight at 65ºC. Then, the different muscle constructs were printed around their specific anchor system using a gelatin-fibrinogen-C2C12 cell-based bioink. After 14 days in differentiation media, all constructs demonstrated good cell viability and matured myotubes. Parallel- and fusiform-shaped constructs showed fibers aligned in parallel, while bipennate constructs exhibited fiber alignment in two directions according to the design. Circular constructs showed concentric fiber alignment. Under electrical pulse stimulation, all constructs contracted along fiber direction. Our results suggest that complex muscle constructs with controlled fiber orientation can be obtained through the implementation of dedicated anchor systems and careful control of the bioprinting process.

POSTER 11 presented by:

NAME: Armando Cortés

Decoding skeletal muscle-liver axis in the context of sarcopenia: Towards the multi organ on a chip

Cortés-Reséndiz, Armando [1], De Chiara, Francesco [1], Ramón Azcón, Javier [1,2]
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Sarcopenia is characterized by marked reductions in skeletal muscle mass and quality, which impacts the mobility and autonomy of patients. They suffer not only from low physical performance and strength but also face a greater risk of falls and further comorbidities, one of those being non-alcoholic steatohepatitis (NASH), as reported by some studies. These have described a correlation between diminished muscle strength and the onset of NASH. Thus, our study examines sarcopenic phenotypes in three-dimensional muscle tissues in contact with conditioned media from NASH.

This approach involves subjecting skeletal muscle tissues to incubation in culture media derived from a pre-established model of NASH. We encapsulated human hepatocytes and hepatic stellate cells (HSC) in a collagen-based hydrogel. After treatment, our model accumulates excess lipids upon a challenge with non-esterified fatty acids (NEFAs), shows activation of HSC, primary drivers of fibrosis, and exhibits a proinflammatory environment. We also show the presence of apoptotic phenotypes and paracrine signaling between cell types of the liver. Such conditions trigger an atrophic phenotype in healthy skeletal muscle tissues, fabricated by encapsulating human myoblasts in a Matrigel and fibrinogen matrix using PDMS casting. Skeletal muscle tissues were functionally evaluated as well by electrical pulse stimulation (EPS). We show that treated tissues exert lower contractile forces during EPS regime compared to our control conditions.

Both of our models pose valuable tools to aid in the identification of potential drug targets and therapeutic strategies, as they mimic key features and cellular microenvironments of sarcopenia and NASH. For this reason, our investigation marks a critical step toward understanding the intricate associations between these diseases. With the multi organ on a chip in sight, we will focus on integrating both models inside an organ-on-chip device.

POSTER 12 presented by:

NAME: Michela Lain Contato

Evaluation of two targeted spatial proteomic platforms: CODEX and MIBI

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Solid tumors are composed of a diverse mixture of cancer, immune, and stromal cells. Understanding their spatial organization within the tumor microenvironment (TME) is critical for deciphering mechanisms of tumor progression and response to therapy. Targeted spatial proteomics for spatial organization studies of the TME is poised to revolutionize clinical practice as a natural evolution of immunohistochemistry (IHC), a technique routinely used for clinical diagnostics. However, direct comparisons that evaluate the relative capabilities and trade-offs of the major available platforms are currently scarce. In this study, we systematically evaluate two leading targeted spatial proteomics platforms: Co-Detection by Indexing (CODEX), a cyclic immunofluorescence technology, and Multiplexed Ion Beam Imaging (MIBI), an imaging mass spectrometry technique. Using a tissue microarray from a clinical cohort of 85 patient-derived head and neck squamous cell carcinoma samples, we processed sequential sections from the same tissue blocks on both platforms. To enable a side-by-side evaluation, we applied a comparable Python pipeline for image pre-processing, segmentation, and iterative clustering. Our results demonstrate that despite inherent differences in sample preparation and imaging approaches, both technologies can yield consistent and spatially relevant biological conclusions. For example, using antibody markers such as CD4, FOXP3, γH2AX, and cytokeratin, we successfully differentiated and localized CD4+ T cells, regulatory T cells, and cancer cells while simultaneously assessing cellular states like DNA damage. Our workflow identified a broad range of cell phenotypes with high resolution, including those tightly packed or morphologically ambiguous. In conclusion, both MIBI and CODEX enable robust multiplexed, spatially resolved characterization of cellular architecture and heterogeneity in the TME. Future work will focus on a deeper spatial characterization of the dataset, alongside a direct comparison of the resolution and dynamic range of the two platforms. Once completed, this study will provide a robust framework for understanding the respective strengths and limitations of each technology, helping researchers select the optimal platform to accelerate the application of spatial biology in cancer research.

POSTER 13 presented by:

NAME: Natalia Castro

Development of personalized bioinks for skeletal muscle tissue engineering to understand the role of the extracellular matrix in Duchenne muscular dystrophy

Castro, Natalia [1], Fernández-Garibay, Xiomara [1], Rodríguez Gallo, Carolina [1], Ramón Azcón, Javier [1, 2], Fernández Costa, Juan M. [1]
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The extra-cellular matrix (ECM) is a network of proteins and other macromolecules that provides biomechanical and biochemical support essential for cellular processes, such as tissue repair. Abnormal changes in ECM are a hallmark of degenerative diseases such as Duchenne muscular dystrophy (DMD). DMD is a rare, genetic, degenerative neuromuscular disorder that causes progressive loss of muscle function. One of the primary challenges in the development of new treatments for the disease is the limited efficacy of current preclinical tools. Three-dimensional (3D) tissue models are an approach that is gaining increasing recognition for their ability to more accurately replicate the structural and functional complexity of native tissues. Tissue engineering employs a variety of different tools for recreating native cellular microenvironments in 3D tissue modeling; however, there is widespread use of animal-derived materials that poses significant challenges for clinical translation. To overcome these limitations, this research aims to develop patient-specific, xeno-free bioinks derived from human ECM to enable the 3D bioprinting of skeletal muscle tissues for disease modeling. This will provide a physiologically relevant model to investigate the role of ECM in DMD and support the development of personalized therapeutic strategies. The ECM is sourced from human fibro-adipogenic progenitor cells (FAPs), which are known for their robust ECM secretion, particularly in muscle tissue repair. FAPs were differentiated towards a fibroblast lineage and cultured with vitamin C to further stimulate ECM deposition. Subsequently, decellularization was optimized using a combination of biological and chemical methods, resulting in the effective removal of cellular components while preserving the integrity of the ECM. This xeno-free, human-derived ECM is being developed as a bioink for 3D bioprinting applications, with the goal of enabling scalable, high-throughput tissue fabrication, reducing the reliance on animal-derived materials, and providing patient-specific models to personalize therapeutic strategies.

POSTER 14 presented by:

NAME: Adriana Lattanzi

Comparative deep mutagenesis of CAPRIN1 to uncover the mechanism by which its pathogenic variant P512L causes neurodevelopmental disorders

Adriana Lattanzi, Benedetta Bolognesi
Institute for Bioengineering of Catalonia (IBEC)

CAPRIN1 is an RNA-binding protein (RBP) highly expressed in the brain. It undergoes phase separation through its intrinsically disordered region and its interaction with G3BP1 facilitates stress granules assembly. Previous studies have highlighted CAPRIN1 association with neurodevelopmental disorders suggesting haploinsufficiency, due to loss-of-function mutations, as a cause (Pavinato et al., 2023). The CAPRIN1 variant P512L has recently been reported in unrelated children affected by early-onset ataxia, cognitive decline, and muscle weakness (Delle Vedove et al., 2022). In human cell lines, overexpression of the wild-type protein results in a diffuse cytoplasmic distribution, whereas its P512L variant forms insoluble aggregates that sequester other proteins implicated in neurodegeneration. Notably, the P512L mutation lies within the prion-like domain (PrD) of CAPRIN1, a feature shared with other proteins involved in neurodegenerative diseases. Moreover, the tendency of this variant to form insoluble aggregates raises the possibility of amyloid formation, similarly to other aggregation-prone proteins involved in disease.

Here, we employed a deep mutational scanning approach to systematically investigate the effects of all 1280 amino acid substitutions within residues 511–550 of CAPRIN1 on its propensity to form amyloids, both in the wild-type background and in the presence of the P512L mutation. While the P512L background increases amyloid formation by 2-fold compared to the wild-type background, our results also highlight the generation of a distinct amyloid core, providing a plausible explanation for the *in vivo* phenotypes resulting from P512L.

Overall, these findings provide the first complete mutational maps of CAPRIN1 revealing mechanistic insights in the aggregation of this protein and its role in neurodegenerative and neurodevelopmental disorders.

POSTER CELL ENGINEERING

POSTER 15 presented by:

NAME: Jaime Casado

In Situ Tracking of Clonal Evolution and Phenotypic Heterogeneity in Tumors by Spatial Epitope Barcoding

Drainas, Alexandros [1]; Casado García-Consuegra, Jaime [2]; Delgado-González, Antonio [1]; Nolan, Garry [1]; Sage, Julien [1]; Rovira-Clavé, Xavier [1,2]
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Understanding how cancer cell subclones adapt to the changing tumor microenvironment is key to designing successful cancer therapies. Combinatorial tagging combined with spatial omics readouts to track barcodes in situ within tissue samples has allowed analyzing the spatial organization of cell lineages and phenotypes in xenograft models of cancer, uncovering emergent behaviors from mixed clones and the selective growth of clonal regions. However, it is still unclear how genetic or chemical perturbations influence subclonal evolution and phenotypic heterogeneity. Here, we incorporated genome editing tools and chemotherapy treatment to a barcoded xenograft model of small cell lung cancer, allowing us to investigate how the interplay between genetic and chemical modifications affect clonal behavior and phenotypic diversity within the tumor microenvironment.
We observed that knocking out certain genes involved in small cell lung cancer progression exhibited distinct growth behaviors, suggesting gene-specific effects on clonal expansion. We identified clear patterns of clonal advantage that varied depending on treatment conditions: in untreated tumors, clones lacking NF2, a tumor suppressor involved in contact inhibition, showed enhanced expansion. Conversely, under cisplatin treatment, clones with SLFN11 knockouts, known to mediate sensitivity to DNA-damaging agents, expanded preferentially. In this context, we observed a structured spatial distribution of clones across both treatment-exposed and phenotypically distinct regions of the tumor, which may play a role in shaping tumor progression. Furthermore, our results revealed diverse interactions between clones under different treatment conditions pointing to a potential role of spatial context and interclonal relationships in modulating clonal behavior in small cell lung cancer. This study underscores a connection between genetic alterations, subclonal dynamics, spatial distribution and chemotherapy response of cancer cells in the tumor microenvironment. The results exemplify the utility of this method in providing new perspectives on the processes driving tumor growth and therapeutic resistance, offering valuable insights for the advancement of personalized cancer treatments.

POSTER 16 presented by:

NAME: Carles Verdaguer

Developing an *in vitro* 3D model to track tumor-macrophage interactions with spatial proteomics

Verdaguer, Carles [1], Casellas, Sergi [1], Rovira-Clavé, Xavier [1]
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Colorectal cancer (CRC) is the second leading cause of cancer-related death worldwide and is characterized by a highly complex and heterogeneous tumor microenvironment. Among the key components of this environment are tumor-associated macrophages (TAMs), which exhibit diverse phenotypes and spatial arrangements, contributing to both pro- and anti-inflammatory responses. Understanding how macrophages respond to tumor-derived cues and how their phenotypes evolve over time remains a significant challenge, in part because of the absence of *in vitro* models that recapitulate this phenomenon. In this work, we are developing a 3D *in vitro* co-culture model composed of HCT116 colorectal cancer spheroids and THP-1-derived macrophages. THP-1 monocytes were differentiated and polarized into M1- or M2-like phenotypes using defined cytokine treatments. Immunofluorescence analysis was used to assess the expression of macrophage markers CD11b, CD14, CD68, and CD163 under various conditions. To enhance physiological relevance, the model was embedded in a gelatin hydrogel that supports 3D structure and cell viability. These experiments are the foundation for the development of a platform providing a controlled system to study tumor-macrophage interactions *in vitro* and may serve as a basis for future efforts aiming to investigate spatial phenotypes and functional plasticity of TAMs in CRC. Ultimately, it contributes to the development of more physiologically relevant tools to explore immune-tumor dynamics and inform therapeutic strategies.

POSTER CELL ENGINEERING

POSTER 17 presented by:

NAME: Aleixandre Rodrigo Navarro

Optogenetic gene expression control in *Lactococcus lactis*

Rodrigo Navarro, Aleixandre[1], Salmeron Sanchez, Manuel
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Lactococcus lactis is a gram-positive bacterium widely used in biotechnological and industrial applications due to its suitability to produce high-value chemicals and recombinant proteins. Multiple chemically inducible gene and protein expression systems have been developed. Here we present a novel inducible system that relies solely blue light, using a combination of small engineered Vivid photoreceptors from Neurospora crassa (Magnets or eMags) and a split mutant T7 RNA polymerase.

Our findings demonstrate that the RNA polymerase is active and non-cytotoxic in *Lactococcus lactis*, and when fused to the Magnets/eMags, it drives gene expression in a light intensity- and time-dependent manner. This marks the first time that a split T7 RNA polymerase fused to photoreceptors has been described in a gram-positive bacterium.

This system provides an attractive alternative to chemically inducible systems since it can be activated by physical stimulus alone, thus avoiding the need to add inducers into the medium and adding a reversibility dimension, enabling the stopping of the expression without the need to remove the inducer from the medium. Furthermore, this system can be applied in various biotechnological applications where precise spatiotemporal control of gene expression is required, especially in the context of living biomaterials where chemical stimuli are diffusion-controlled, difficult to switch off and thus cannot be applied locally in a reversible way, a role where light excels. We foresee potential applications in tissue engineering and industrial protein production.

POSTER 18 presented by:

NAME: Júlia Fabà Costa

An ex utero embryo culture platform to address peri-implantation development

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Infertility affects around 15% of reproductive-aged couples worldwide. One of the critical points for pregnancy progression is embryo implantation, since the majority of unsuccessful conceptions are lost in this step and only one third of conceptions progress and lead to a live birth. This natural inefficiency of human implantation has not been significantly improved with the arrival of assisted reproductive techniques. Therefore, in order to overcome this roadblock in human reproduction, we need a deeper understanding of the sequences of events that control the formation and progression of the human conceptus during implantation.

The current embryo culture technology patches different stages of embryo development, ranging from preimplantation stages to early organogenesis. But, so far, nobody has accomplished a continuous culture from zygote all the way until organogenesis. The static culture conditions used in those systems, where the distribution of nutrients and gases depends only on passive diffusion, is one of the limiting factors.

Here, we propose an embryonic culture platform integrated into a microfluidic device which allows us to apply a flow of media to the culture system. These features enable us to adapt both gases and nutrient supply to the developmental stage of the embryos, while also facilitating the removal of waste products. The device is fabricated by replica molding and consists of a culture platform with an integrated hydrogel layer on which the embryos can implant.

Fabrication and sterilization protocols have been adapted to host mouse embryos. They have been cultured from blastocyst stage (day 4.5 after fertilization) to early-gastrulation stage after 4 days of culture in the device. Embryos have an implantation morphology similar to those shown in literature, and express Oct4, a marker of the embryonic epiblast, precursor to the future fetus, and Cdx2, a marker of the trophectoderm, the extraembryonic tissue precursor of the placenta.

The platform is currently under adaptation and validation for human embryo culture, aiming to enable the study of implantation and development from blastocyst to pre-gastrulation stages under dynamic and controlled conditions.

Altogether, we have engineered a microfluidic platform that will help us to study mouse and human embryo implantation under controlled culture conditions, enabling us to investigate embryo development from zygote to post-gastrulation stages.

POSTER | CELL ENGINEERING

POSTER 19 presented by:

NAME: Victoria Batto

Immunosuppressive microenvironment shaped by collagen dynamics in lung adenocarcinoma

Victoria Batto[1,2], Enrico Almici[2], Marselina Arshakyan[1], Neel I. Nissen[3], Nicholas Willumsen[3], Noemí Reguart[4], Josep Samitier[2], Morten Karsdal[3], Jordi Alcaraz[1,2,4]

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The tumor stroma rich in fibrillar collagens plays a critical role in non-small cell lung cancer (NSCLC) progression and immune evasion. To understand the complex collagen-dependent immunosuppressive processes, we analyzed collagen expression, organization and degradation in relation to major immune cell populations and regulators in patient samples and patient-derived tumor-associated fibroblasts (TAFs) from lung adenocarcinoma (ADC) and squamous cell carcinoma (SCC).

Histological analysis of fibrillar collagens stained by picrosirius-red (PSR) and cancer-relevant immune cell types (T-cells, Tregs, macrophages) showed a negative correlation between PSR stain and CD8+ T-cells selectively in ADC, supporting that collagen may promote cytotoxic T-cell exclusion in ADC. Collagen organization, assessed by polarized light imaging and CT-FIRE analysis, revealed longer, straighter, and more aligned fibers in tumors compared to paired samples from uninvolved pulmonary tissue, particularly in ADC, indicating increased tumor stiffening. Consistently, stiffness-associated processes, including fibroblast activation (α-SMA) and immune evasion (PD-L1), were upregulated in the high collagen fiber density patient group selectively in ADC. Notably, high collagen fiber density correlated with worse survival in both ADC and SCC independently of TNM-staging, while fiber alignment predicted better prognosis only in ADC.

In vitro studies using TGF-β1-activated TAFs revealed increased production of soluble collagen fragments in SCC-TAFs compared to ADC-TAFs, particularly collagen I, III and VI. Among them, type III collagen pro-peptide (PRO-C3) has been consistently associated with poor overall survival (OS) in different solid tumors. Moreover, TCGA whole-tumor RNA analysis revealed increased expression of collagenases in SCC compared to ADC, collectively supporting a larger collagen degradation in SCC that could favor tumor progression. These observations shed light on the complex contributions of collagen turnover and architecture to immune evasion, and how they may depend on the histology in NSCLC. Moreover, they highlight the necessity to include collagen and related biomarkers in clinical studies of immuno-oncology for improved patient stratification and personalized therapeutic approaches.

POSTER 20 presented by:

NAME: Anisha Pahuja

Exploiting human pluripotent stem cells to study human disease in kidney and retina

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Congenital anomalies of the kidney and urinary tract (CAKUT) encompass a broad spectrum of structural and functional malformations caused by genetic and environmental disruptions during embryonic development. While mouse models have identified several genes involved in CAKUT, species-specific developmental differences limit the direct translation of these findings to human biology. Human pluripotent stem cell (hPSC)-derived organoids offer a promising platform to study early morphogenetic events related to CAKUT manifestation.

Our project aims to utilize hPSC-derived organoids to model human kidney development and CAKUT. In this regard, we are making use of our established protocol to generate kidney organoids derived from stable knock-out cell lines made using CRISPR-Cas 9 technology to dissect the role of LHX1, a key transcription factor involved in intermediate mesoderm induction and renal progenitor specification. LHX1-null organoids exhibit profound morphogenetic defects, including complete loss of renal vesicles and nephron-like structures. RT-qPCR and immunofluorescence analyses reveal downregulation of Notch pathway effectors (e.g., DLL1, JAG1) and renal identity markers (PAX2, PODXL, WT1), corroborated by hematoxylin-eosin staining that shows disorganized tissue architecture.

To explore potential extra-renal manifestations, we also differentiated LHX1 knock-out hPSCs into retinal-cup organoids. Despite the absence of LHX1, these organoids retained the ability to form major retinal layers, as demonstrated by immunofluorescence and RT-qPCR for retinal markers (SIX3, CRX, OTX2). These findings suggest that early retinal differentiation is not overtly impaired by LHX1 loss, although further investigation is needed to assess potential later-stage or functional consequences.

Additionally, we are engineering microfluidic platforms via soft lithography to deliver spatially and temporally controlled biochemical and biophysical cues, further enhancing organoid patterning and maturation.

Together, this multidisciplinary approach offers new insights into both renal and extra-renal manifestations of CAKUT and potentially inform future therapeutic strategies.

POSTER CELL ENGINEERING

POSTER 21 presented by:

NAME: Vladislav Petrovskii

Ordering competition drives tunable properties in cell-mimicking membranes

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Controlling the properties of cell-mimicking systems remains a challenging task, especially when they must meet mutually exclusive requirements such as high stability and flexibility. Recently, ionically linked comb polymers (iCPs) have been introduced. These combs consist of a polyelectrolyte backbone made of zwitterionic and cationic monomers; to the latter, anionic ligands are appended. This system can self-assemble into giant unilamellar vesicles with very promising properties: biomimetic membrane thickness, high flexibility, and lateral mobility. While these vesicles resemble polymersomes, they are more closely related to polyelectrolyte–surfactact complexes. This behavior is likely due to the unique topology of iCPs, which leads to the formation of a true ligand bilayer flanked by cationic polyelectrolytes. The polyelectrolytes are constrained into a quasi-2D configuration, which reduces their entropy and results in nematic ordering of the chains. Using a molecular dynamics approach, we varied the degree of polymerization or the composition of co-monomers in the backbone. Remarkably, the membrane quality remains consistent across a wide range of studied parameters. The bending rigidity can be modulated by nearly an order of magnitude, while lateral mobility remains within the same order and is comparable to that of liposomes. Membrane thickness also stays within a narrow range from 5 to 12 nm. These membrane properties are governed by the competition between ligands and backbones via electrostatic interactions. Interestingly, we also found that their ordering is inversely related, offering an additional strategy to fine-tune the properties of i-combisomes.

POSTER 22 presented by:

NAME: Karolina Zimkowska

AAV-Driven P301L-Tau Expression Modulates Neuronal Activity in Human Cortical Brain Organoids

Karolina Zimkowska [1,2,3,4], Marc Riu-Villanueva [1,2,3,4], Eduardo Yanac-Huertas [1], Irene Fernández-Carasa [5,6], Jorge Oliver-De La Cruz [7], Antonella Consiglio [5,6], Jordi Soriano [8,9] and José A. del Río [1,2,3,4]

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Microtubule-associated protein tau is crucial in neuronal health by influencing axonal transport and microtubule stabilisation. In contrast, pathological tau is associated with early cognitive decline in pure tauopathies, such as Frontotemporal Dementia with Parkinsonism linked to chromosome 17 (FTDP-17). Although rare in the general population, the P301L mutation accounts for approximately 25-40% of familial FTDP-17 cases with confirmed MAPT mutations. Tau pathology in P301L-associated tauopathies primarily impacts excitatory glutamatergic neurons and astrocytes, contributing to synaptic loss, impaired neuronal connectivity, and glial dysfunction. These disruptions ultimately compromise network integrity and cognitive-emotional processing, aligning with the clinical phenotypes observed in affected individuals. Furthermore, research shows that endogenous tau is implicated in neuronal activity (NA), although the role of tau in this process is poorly understood. Neuronal excitation also regulates tau by promoting extracellular release and phosphorylation. In this respect, changes in NA in the presence of tau mutations have not yet been analysed at presymptomatic stages.

To address this, we present an *in vitro* platform utilising semi-guided cortical brain organoids (CBOs) derived from hPSCs to unravel the impact of tau pathology on NA by exploring the changes that occur after the inclusion of mutated P301L-tau or full-length non-mutated human tau (2N4R) by adeno-associated virus. This system enables a high-resolution investigation of tau aggregation, neurotoxicity, and network-level perturbations within a human-relevant three-dimensional context. Through overexpression of P301L-tau, we successfully developed hCBOs that exhibit an increased ratio of 4R in the 4R/3R tau expression, hyperphosphorylated tau as observed by biochemical analysis of ptau(Ser422) and AT8, as well as tau aggregates observed by positive staining for MC1 antibodies. Additionally, we have shown that these hCBOs have changes in neuron firing frequency and neuronal network properties between P301L-tau, 2N4R-tau, and control hCBOs. This model can, therefore, be used to further explore the functional consequences of tau mutation-mediated changes of NA in tauopathies.

Our findings not only illuminate the pathogenic cascade triggered by the P301L mutation but also lay the foundation for testing therapeutic strategies targeting tau-driven neurodegeneration in a human-derived, disease-relevant model.

POSTER CELL ENGINEERING

POSTER 23 presented by:

NAME: Inés Martínez

Role of GPR133 in Modulating Neuronal Susceptibility and Synaptic Plasticity: Insights from a Knockout Mouse Model

Inés Martínez-Soria [1,2,3,4], Pol Picón-Pagès [1,2,3,4*], Núria Moral [5], Anna P. Pérez-González[6,7], Elena De Cecco[8], Jordi Duran [1,3,5], Xavier Gasull [6,7], Adriano Aguzzi [8], Rosalina Gavín [1,2,3,4], José Antonio del Río [1,2,3,4]*

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The adhesion G protein-coupled receptor GPR133 (Adgrd1) has been implicated as a potential modulator of key neuronal processes. Our project investigated its role in neuronal development, synaptic plasticity and neurodegeneration. A mouse model deficient in Adgrd1 (Adgrd10/0) was used in combination with histological, molecular, electrophysiological and behavioural techniques. Adgrd10/0 mice exhibited heightened susceptibility to kainate (KA)-induced excitotoxicity, which was associated with early neurodegeneration of principal pyramidal neurons in the hippocampal stratum pyramidale, along with enhanced glial reactivity and increased neuroinflammation. RT-qPCR analysis of hippocampal tissue from mutant animals revealed a significant overexpression of the Grik3 gene, which encodes a subunit of the KA receptor (KAR). Behaviourally, these mice showed reduced exploratory activity and impaired nest-building. In addition, electrophysiological recordings in adult hippocampal slices revealed a trend toward reduced long-term potentiation (LTP), although dendritic spine density remained unchanged. To explore long-term effects of excitotoxic damage, additional experiments combined KA administration with 5'-bromo-2'-deoxyuridine (BrdU) injections to label proliferating cells. These studies aimed to assess neurogenesis and cellular proliferation in the hippocampus several days post-injury, providing insight into the regenerative capacity and response to damage in Adgrd10/0 mice. In addition to the previously completed tests, further behavioural assessments were carried out to investigate a potential lack-of-motivation phenotype in Adgrd10/0 mice. These included the Y-maze and marble burying test, commonly used to evaluate anxiety-like behaviour, compulsivity and motivational impairments. The results of these assays provided additional insights into whether the reduced exploratory activity and poor nest-building performance previously observed could be linked to diminished motivation in this knockout model. In summary, these findings provide compelling evidence that the absence of GPR133 increases neuronal vulnerability to excitotoxic damage. This heightened susceptibility is accompanied by more pronounced neuronal injury, functional deficits, and behavioural alterations, phenomena not observed in animals expressing GPR133, highlighting its critical protective role.

POSTER 24 presented by:

NAME: Luciano Riso

Tuning cryogel pore orientation for mimicking cartilage architecture

Luciano Riso [1]; Cosimo Loffreda [2]; Andrea Barbero [3]; Florian Thieringer [4]; Fabiana Arduini [5]; Valentina Basoli [2]; Javier Ramón [1,6]
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Introduction: Cartilage regeneration remains a significant challenge due to its complex, multilayered architecture characterized by distinct orientations, functions, and mechanical properties. While hydrogels have been extensively studied for their potential to enhance chondrocyte differentiation, they often exhibit limitations in porosity and directional control. Cryogels, with their highly tunable and interconnected porous structures, offer an innovative approach to face these challenges. This study aims to fabricate cryogels with controlled pore orientation and assess their biocompatibility for cartilage tissue engineering applications.

Materials & Methods: Cryogels were synthesized using a 2% (w/v) gelatin from porcine skin and 2% (w/v) sodium carboxymethyl cellulose (CMC) solution, crosslinked with adipic acid dihydrazide (AAD) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC). Fluoresceinamine 1mM was added for initial pore visualization. The prepolymerized solution was injected into polydimethylsiloxane (PDMS) molds to ensure reproducible geometry. After initial crosslinking gels were subjected to isotropic or anisotropic freezing at –20 °C to generate distinct pore architectures. Pore formation was initially visualized via fluorescence microscopy, and structural characterization was performed using scanning electron microscopy (SEM). Biocompatibility was evaluated through LIVE/DEAD assays on human chondrocytes isolated from three patients that underwent total knee replacement.

Results: Fluorescence microscopy confirmed successful pore incorporation, while SEM analysis revealed differential pore orientation for each freezing condition. Isotropic freezing produced randomly oriented pores, whereas anisotropic freezing yielded vertically aligned structures. These structures resemble the architecture of the native cartilage transitional and deep zones, respectively. The fabrication protocol demonstrated high reproducibility across batches. Both random and unidirectional cryogels showed to be biocompatible as assessed by chondrocyte adhesion and survival over seven days.

Conclusion: Random and aligned pore structures in tunable cryogels are particularly promising for directing cell orientation and extracellular matrix organization, which are key to achieving a functional cartilage layer. Future studies will focus on refining the cell seeding protocol and evaluating the long-term performance of these scaffolds in promoting stable and functional cartilage.

POSTER | CELL ENGINEERING

POSTER 25 presented by:

NAME: Nuria Moral

Uncovering the Role of Glycogen in GABAergic Interneurons in Lafora Disease-Associated Epilepsy

Núria Moral [1], Inés Martínez-Soria [2,3,4,5], Pol Picón-Pagès [2,3,4,5], José Antonio del Río [2,3,4,5], Jordi Duran [1,2,3]
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Lafora disease is a rare metabolic neurodegenerative disorder characterized by the accumulation of abnormal glycogen aggregates in several tissues, including the brain. This condition, which affects adolescents, manifests as a severe form of progressive myoclonic epilepsy, marked by relentless seizures and rapid neurodegeneration. The disease represents a significant medical challenge due to its intricate molecular mechanisms and the limited efficacy of available therapeutic interventions

We previously demonstrated that glycogen aggregates in Lafora disease accumulate both in neurons and astrocytes, and that astrocytic aggregates induce neuroinflammation. Our current research has led to the identification of a previously unrecognized role of glycogen within GABAergic interneurons, key regulators of neuronal excitability and inhibition. By employing *in vivo* models with altered glycogen metabolism, we show that abnormal glycogen accumulation in these interneurons contributes to the onset and progression of epileptic seizures in affected individuals. Specifically, we have observed disruptions in GABAergic signaling pathways, resulting in dysregulated inhibitory neurotransmission and heightened neuronal excitability, culminating in seizure activity.

Our study not only deepens our understanding of the metabolic causes of epilepsy in Lafora disease but also highlights the potential therapeutic targets within the glycogen metabolism pathway. By elucidating the intricate metabolic interactions between glycogen and neuronal function, our findings pave the way for the development of targeted interventions aimed at restoring metabolic homeostasis and alleviating epilepsy symptoms in affected individuals. Importantly, these results might have implications for the etiology of epilepsy beyond Lafora disease.

POSTER 26 presented by:

NAME: Yunuen Avalos Padilla

Disruption of proteostasis and growth impairment in *Plasmodium falciparum* by an Intrinsically disordered PfUT segment

Yunuen Avalos-Padilla [1,2], Inés Bouzón-Arnáiz [1,2], Miriam Ramírez [1], Elsa M. Arce [3], Diego Muñoz-Torrero [3,4], and Xavier Fernàndez-Busquets [1,2,5].

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The *Plasmodium falciparum* proteome shows a strong tendency toward aggregation, driven by its AT-rich genome, which encodes many proteins with long asparagine-rich stretches and low structural complexity. These features give rise to abundant intrinsically disordered regions. While protein aggregation poses challenges for the parasite, it may also serve adaptive functions during stress. At the same time, this trait represents a potential vulnerability that could be therapeutically targeted.

In this study, we overexpressed an aggregation-prone segment of the *P. falciparum* ubiquitin transferase (PfUTf), an E3 ubiquitin ligase involved in regulating the stability of proteins linked to invasion, development, and drug metabolism. PfUTf overexpression in parasites led to marked phenotypic changes, as revealed by transmission electron microscopy and confocal fluorescence imaging. It impaired parasite growth, increased endogenous protein aggregation, and disrupted proteostasis. When combined with dihydroartemisinin treatment, PfUTf overexpression produced a synergistic effect, further decreasing parasite viability and linking protein aggregation to proteasome dysfunction.

Additionally, altered distribution patterns of aggregation-prone proteins were detected using the investigational anti-aggregative compound YAT2150 in PfUTf-overexpressing parasites. Together, these findings underscore the delicate balance between protein aggregation, stress responses, and parasite survival, and support targeting proteostasis as a promising antimalarial strategy.

POSTER 27 presented by:

NAME: Lluis Mangas Florencio

Parallel Cellular Metabolic Imaging by Merging MRI and Microfluidics for Personalised Medicine

David Gomez-Cabeza [1], Lluis Mangas-Florencio [1], Marc Azagra [1], Alba Herrero-Gomez [1], James Eills [1], Alejandro Portela [1], Gergo Matajsz 1 Irene Marco-Rius [1]

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The complex metabolic profile of multiple diseases urges researchers to find novel and personalised approaches to understand and treat them. To meet this demand, advanced *in vitro* technologies are developed to replicate human physiology and metabolism. Organs-on-a-chip (OoC) emerged as a promising platform to mimic key architecture and functionality of organs[1]. Such systems proved an opportunity to develop complex patient-derived models for disease research[2].

To fully exploit OoCs potential for metabolic research, it's essential to combine them with methodologies capable of capturing real time biochemical dynamics. Magnetic Resonance (MR) enables the analysis of molecular composition and dynamics, yet hampered by low sensitivity. 13C nuclear spin hyperpolarization (HP) techniques enhance signal intensity by 10,000-fold[3]. In this work, we combine OoC with HP-MR spectroscopic imaging to study the cellular metabolism in real-time and non-destructively in a parallel manner.

To emphasise the broad applicability of our work, we designed PDMS microfluidic systems with one inlet distributing HP substrate to measurement chambers. Here, we measured and characterised the dysregulated flux from HP-[1-13C]pyruvate to HP-[1-13C]lactate characteristic of the Warburg effect in HepG2 and HeLa cells. In a 3T MRI scanner (Bruker), we used chemical shift images (CSI) for static spatially resolved measurements or sequential selective single pulses (SSSP) for temporal data.

Using CSI, we successfully differentiated the metabolism of HepG2 and HeLa cells. We also investigated the metabolic activity changes induced by media composition and cell membrane integrity to characterise the system. Next, we induced lactate production modulations using reaction inhibitors, validating the potential of this platform for personalised medicine.

In addition, we measured with SSSP a 3D model of HepG2 cells as an advancement towards developing more complex *in vitro* models. This 3D model embedded in our OOCs allowed us to conduct longitudinal studies thanks to media recirculation. While we need to improve sensitivity, the platform presents an enticing system for drug testing in a longitudinal, non-invasive, and non-destructive fashion.

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POSTER 28 presented by:

NAME: Francisco Manuel Sáez González

Humanized Models for Studying Spinal Cord Injury and Developing Therapeutic Strategies

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Spinal cord injury (SCI) is a devastating condition that causes permanent motor and sensory impairment and remains a major clinical challenge due to the absence of effective regenerative therapies and the poor translatability of current preclinical models. Significant anatomical and physiological differences between humans and commonly used animal models hinder the development of successful interventions. To address this gap, the current study focuses on developing advanced humanized *in vitro* and *in vivo* spinal cord injury models that better capture the complexity of the human nervous system aiming to improve our understanding of SCI and enhance the translational potential of candidate therapies. The study proposes the use of human induced pluripotent stem cell (iPSC)-derived spinal cord organoids (hSCOs) fused with vascular organoids (hVOs) to generate vascularized spinal cord organoids (hVSCOs) as a more physiologically relevant model of the human spinal cord. The group has effectively established both hSCOs and hVOs comprising disease-relevant cell types of neural, vascular, and neuroimmune lineages and has demonstrated successful fusion at multiple hSCO developmental stages, as evidenced by the integration of blood vessels within neural tissue. Moreover, preliminary results following the induction of a controlled mechanical injury in hVSCOs reveal hallmark features of SCI, including glial reactivity, neuronal degeneration, and vascular disruption, as assessed by immunohistochemistry, along with a notable decline in electrophysiological activity recorded via multielectrode arrays (MEA). In parallel with the in vitro approach, a humanized mouse model is being established by transplanting hSCOs into the spinal cord of immunodeficient juvenile mice to replicate key features of human injury responses, such as glial scar formation, axonal degeneration, and neuronal plasticity in an *in vivo* context. These models enable the study of human-specific mechanisms underlying spinal cord injury and provide a platform to investigate other neurological conditions and diseases.

Key words: Spinal Cord Injury (SCI), Humanized Preclinical Models, Human Spinal Cord (hSCOs) and Vascular Organoids (hVOs), vascularization.

POSTER CELL ENGINEERING

POSTER 29 presented by:

NAME: Dayaneth Jácome

3D Glioblastoma Spheroid Model for Natural Hypoxia Induction to Investigate microRNA-Based Therapeutic Strategies Targeting PrPC Overexpression

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Glioblastoma multiforme (GBM) is among the most lethal human cancers, and the prognosis for affected individuals remains extremely poor. Current therapies are largely ineffective due to several critical challenges, including the late detection of the tumor, its rapid infiltration into brain parenchyma that complicates surgical removal, and the presence of the blood-brain barrier, which restricts drug bioavailability and facilitates immune evasion, among other factors.

The overexpression of the Cellular Prion Protein (PrPC) in GBM—associated with hypoxic conditions—is known to further worsen prognosis and contribute to therapeutic resistance. Elevated PrPC expression has been reported in various tumor types, where it enhances tumorigenic potential, proliferation, and invasion through pathways such as STI-1, Bcl-2, and GSK3-Wnt, among others.

Therefore, the controlled downregulation of PrPC expression represents a promising strategy to enhance therapeutic approaches in GBM. To investigate this, an *in vitro* model that replicates PrPC overexpression under hypoxic conditions is essential. In our study, we utilize spheroids derived from the U87 glioblastoma cell line, which offer a significant advantage over traditional 2D models by naturally developing tumor-like hypoxia, eliminating the need for artificial induction.

To target PrPC overexpression, we employ a miR-519a-3p mimic, whose ability to downregulate PrPC has been previously demonstrated, along with its reduced expression levels observed in GBM. Restoring miR-519a-3p expression has shown promising outcomes, including decreased tumor proliferation, enhanced chemosensitivity, and reduced metastatic capacity, primarily through inhibition of the STAT/Bcl-2 pathway. miRNA-based therapies hold great potential to advance oncology by enabling personalized treatment strategies tailored to the specific miRNA expression profiles of individual tumors.

POSTER 30 presented by:

NAME: Joel Àlvarez Puig

Studying the interactions of prosthetic joint infection associated pathogens in a *Galleria mellonella* infection model

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Polymicrobial infections are gaining more and more recognition in the clinical context. In the case of device-related infections and deep tissue infections, S. epidermidis and C. acnes are often co-isolated. These species have traditionally been viewed as normal members of a healthy skin microbiome. However, their common occurrence in periprosthetic joint infection, osteomyelitis, and other device-related infections underlines their clinical relevance. This points towards the need to develop experimental *in vitro* and *in vivo* systems that are better capable to understand these polymicrobial infections in an *in vivo* setting, including the potential interactions between species.

In this study, we developed an *in vivo* model for the polymicrobial infection of S. epidermidis and C. acnes using *Galleria mellonella* larvae. This model is easy to use, has low maintenance costs, and has an innate immune system that shares similarities with that of mammals. Additionally, it offers the possibility of using large sample sizes and to incubate the larvae at human body temperature. All of this makes it an excellent model for early-stage studies of infections. With this model, we demonstrated that co-infection with both bacteria increases the mortality of the larvae compared to single-species infections.

A better understanding of polymicrobial infection is crucial for improving the outcomes of patients that suffer them. That is why developing *in vivo* and *in vitro* models that help us better understand complex infections such as those caused by C. acnes and S. epidermidis is important to be able to develop new and better therapies against them.

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POSTER CELL ENGINEERING

POSTER 31 presented by:

NAME: Palash Chandravanshi

Engineering ECM-Mimetic Platforms for Functional Maturation of iPSC-Derived Motor Neurons in 3D Printed Spinal Cord Constructs

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The extracellular matrix (ECM) is a fundamental component of the central nervous system (CNS), playing a key role in neuronal maturation, signalling, and plasticity. However, the complexity of neuronal maturation is not adequately replicated by most *in vitro* human models, which limits their use in the study of CNS injury, disease, and regenerative therapies. To address this issue, our aim was to design an ECM-mimetic microenvironment by identifying and incorporating developmentally relevant cues from the spinal cord ECM. This would enhance the maturation of human induced pluripotent stem cell (hiPSC)-derived neurons in both 2D and 3D printed systems.

Spinal cords from neonatal and adult mice were decellularized using a combination of detergents and mechanical agitation. The resulting decellularized ECM (dECM) was used to coat coverslips, onto which iPSC-derived motor neurons were seeded. Morphometric and electrophysiological analyses revealed distinct differences in neuronal maturation between the two types of substrate. Proteomic profiling of ECM-enriched spinal cord fractions identified three key perineuronal net (PNN) components —Tenascin-R, Versican, and HAPLN1— as candidates for further study. Recombinant forms of these proteins were then used to treat hiPSC-derived neurons in 2D cultures, resulting in significantly enhancing their functional maturation.

To validate this in 3D, we fabricated human-sized spinal cord scaffolds using volumetric 3D bioprinting, combining the three PNN proteins with hyaluronic acid to formulate ECM-mimetic hydrogels. When seeded with iPSC-derived motor neurons, these 3D constructs promoted robust functional maturation, as confirmed by morphological and electrophysiological assays.

In summary, our findings demonstrate that ECM-mimetic hydrogels incorporating key matrisomal proteins can effectively promote the maturation and functional integration of human motor neurons. This approach advances the development of physiologically relevant CNS models and highlights matrisomal analysis as a powerful tool for discovering therapeutic candidates for neurological disorders.

POSTER 32 presented by:

NAME: Chiara Ninfali

Modeling fibrosis and muscle function in Duchenne Muscular Dystrophy (DMD) using an engineered 3D Co-Culture system.

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Duchenne muscular dystrophy (DMD) is a rare neuromuscular disorder marked by the progressive replacement of muscle fibers with fibrotic tissue, caused by the muscle's inability to regenerate properly. Fibro-adipogenic progenitors (FAPs) play a central role in driving this fibrosis, therefore understanding how FAPs contribute to disease progression is essential for developing targeted therapies. In this study, we developed a functional 3D model of human skeletal muscle using 3D-printed casting molds. We encapsulated myogenic precursors from healthy donors with FAPs derived from either healthy individuals or DMD patients (three FAP lines per condition). Including different donors allowed us to account for patient-specific variability and to assess the impact of FAPs on muscle physiology. The engineered tissues formed contractile, functional muscles capable of responding to electrical stimulation. Despite biological variability, we observed a significant reduction in muscle contractile force when myoblasts were co-cultured with DMD-derived FAPs. To investigate the molecular mechanisms underlying this dysfunction, we performed bulk RNA sequencing. Co-culture with DMD-FAPs led to widespread transcriptional changes, particularly in pathways related to extracellular matrix remodeling, fibrosis, and muscle structure and contraction. We also quantified collagen deposition—a hallmark of fibrosis—and found it significantly increased in the DMD-FAP co-cultures. Finally, we used the model to test the efficacy of antifibrotic compounds. This model provides a reliable system to explore novel therapeutic pathways and evaluate antifibrotic drug candidates for muscular dystrophies.

POSTER 33 presented by:

NAME: Eduard Torrents

FleQ-Dependent Regulation of the Ribonucleotide Reductase Repressor nrdR in *Pseudomonas aeruginosa* During Biofilm Growth and Infection

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Ribonucleotide reductases (RNRs) are essential enzymes that catalyze the conversion of ribonucleotides to deoxyribonucleotides (dNTPs), a critical step in DNA synthesis and repair. While all organisms encode for at least one RNR class, *Pseudomonas aeruginosa* harbors three, providing a competitive advantage that allows it to adapt and colonize various environments. Despite their importance, the mechanisms coordinating the expression of different RNRs in microorganisms with multiple RNR classes remain poorly understood. The transcriptional regulator NrdR controls the expression of all three RNR classes by binding to conserved motifs (NrdR boxes) in their promoters. However, the regulation of nrdR itself remains unknown.

In this study, we investigated the transcriptional regulation of nrdR using a combination of bioinformatics and experimental approaches we identified potential transcription factors (TF) involved in nrdR regulation. Our analysis identified four potential TF that could regulate nrdR, and we experimentally confirmed that specifically, FleQ is responsible for regulating nrdR expression under aerobic and anaerobic conditions. Furthermore, we explored nrdR regulation under biofilm-forming conditions and in the *Galleria mellonella* infection model to gain insights into how nrdR might be regulated *in vivo*.

POSTER 34 presented by:

NAME: David Bartolomé Català

Advanced *in vitro* models show tumor modulation of T cell migration in colorectal cancer microenvironments

David Bartolomé-Català [1], Pau Canaleta [1], Jordi Comelles [1, 2], María García-Díaz [1, 2], and Elena Martínez [1, 2, 3]
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Colorectal cancer (CRC) is a leading cause of cancer death worldwide, with T lymphocytes playing a key role by infiltrating tumors and killing cancer cells. While *in vivo* models have advanced our understanding of T cell–tumor interactions, their complexity limits real-time observation of T cell migration. This has driven interest in developing *in vitro* models that better mimic the tumor microenvironment, though replicating *in vivo* complexity remains a major challenge. Here, we present advanced *in vitro* approaches to study T cell migration in the context of CRC, incorporating key elements such as the endothelial barrier, stromal compartment, and tumor epithelium. Using mouse colon organoids derived from wild type (WT) and APC-/- mice, we demonstrate that the tumor environment changes the migratory patterns of T cells. Our study incorporates two complementary *in vitro* systems: (1) Transwell based model mimicking transendothelial migration, where we observed that APC-/- colonoid-derived conditioned medium decreases the total number of T cells crossing the barrier, and (2) A 3D coculture system mimicking the stromal migration embedding T cells and colonoids in a collagen/Matrigel hydrogel. $APC^{-/-}$ signaling altered T cell movement parameters, including distance, spatial coverage, and turning angles. Using a persistent random walk model to describe the migratory behavior of T cells in both environments we highlight how tumor-derived factors reshape T cell migratory behavior and provide insights into the bio-physical dynamics of immune-tumor interactions.

POSTER 35 presented by:

NAME: Serafima Beletskaya

Identifying the Key Factors of Matrisome Remodeling for Spinal Cord Injury Treatment

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The matrisome plays a pivotal role in the structural and biochemical support of the spinal cord tissue. Following spinal cord injury (SCI), the matrisome undergoes significant remodeling, differing markedly between the acute phase, characterized by inflammation and cellular damage, and the chronic phase, where scar formation and inhibitory matrisome components impede regeneration [1]. Advancements in omics technologies, including single-cell RNA sequencing (scRNA-Seq) and proteomics, have enabled comprehensive profiling of these dynamic changes, providing insights into the molecular mechanisms underlying SCI progression. In this study, we integrate 5 publicly available scRNA-seq datasets spanning acute (e.g., day 7 post-SCI) and sub-chronic (e.g., 4-6 weeks post-SCI) stages to generate a high-resolution, cell type–specific transcriptomic atlas of ECM gene expression. These findings are corroborated with quantitative proteomic profiling via DIA-MS performed on the samples prepared at the lab, capturing 297 matrisome-associated protein groups across distinct injury phases. Differential expression analyses enabled ranking and functional annotation of key ECM regulators that modulate injury progression, with top candidates enriched in terms associated with biological processes such as regeneration, axon guidance, and synapse formation. The commercially available ECM proteins identified in the present analysis are being validated using a microphysiological device with an aspiration SCI model. Our multi-omic approach and experimental evidence lay the groundwork for the rational design of biomimetic scaffolds that emulate native ECM environments and support neural repair in SCI [2,3].

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FLASH 36 presented by:

NAME: Mehdi Torabi Goodarzi

VCSEL technology integration into plasmonic biosensors for miniaturized, low cost and portable systems

Torabi Goodarzi, Mehdi [1], Ruiz Gutiérrez, Martín [1], Ramón Azcón, Javier [1,2]

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The integration of Vertical-Cavity Surface-Emitting Lasers (VCSELs) with surface plasmon resonance (SPR) biosensors presents a transformative opportunity for creating compact, multiplexed, low-power, and cost-effective miniaturized diagnostic platforms. SPR is a powerful, label-free technique for real-time biomolecular interaction analysis, but traditional SPR systems are often bulky and expensive due to the use of large light sources, costly spectrometers and complex optical arrangements. VCSELs, with their unique advantages, including micro-scale size, low power consumption, narrow linewidth, high beam quality, wavelength stability, and ease of integration, are well-suited to address these limitations.

However, realizing this potential requires overcoming several technical challenges, including spectral mismatch between VCSEL emission and SPR resonance conditions, inadequate beam profile and polarization for efficient plasmon excitation, thermal wavelength drift, and optical coupling inefficiencies with plasmonic structures. Additionally, one of the major technical barriers lies in the design and fabrication of plasmonic nanostructures that can effectively couple with the specific emission wavelength and mode characteristics of VCSELs.

This study focuses on addressing these limitations by developing a robust integration strategy that includes the use of wavelength-stabilized and polarization-optimized VCSELs, compact optical conditioning elements, precise alignment methods for efficient plasmonic excitation and the development of custom-engineered plasmonic nanostructures tailored to VCSEL operation wavelengths. The resulting miniaturized SPR biosensing platform maintains high sensitivity and stability while significantly reducing size and complexity. Furthermore, the compact and modular design of the developed system allows seamless integration with organ-on-chip platforms, enabling real-time, label-free biomolecular interaction analysis in physiologically relevant microenvironments. This advancement lays the foundation for next-generation, lab-on-chip diagnostic technologies tailored for point-of-care applications and dynamic biological studies.

POSTER 37 presented by:

NAME: David Esteban Suárez Baquero

2P-FENDO: A Flexible Fiberscope for Investigating Inter-regional Brain Circuits in Freely Behaving Animals

Esteban Suárez-Baquero [1], Yoel Melul Steinfeld [1], Nicolò Accanto [1]
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To understand the neural basis of disorders like Post-Traumatic Stress Disorder (PTSD), it is crucial to study the dialogue between brain regions as they operate during natural behavior. This demands tools that can simultaneously monitor and manipulate neural ensembles in different areas with cellular precision in freely moving animals, a significant technological challenge. We developed 2P-FENDO to address this gap. It is a flexible two-photon (2P) fiberscope for all-optical investigation.

The system's primary capabilities include high-speed calcium imaging and precise holographic photostimulation. A key feature is the use of the fiber's intrinsic inter-core delay dispersion (ICDD), which maintains high axial resolution (<9 µm) even with large excitation spots (10-20 µm). 2P-FENDO reliably images at 20 Hz (up to 50 Hz) and, for the first time, enables multi-target 2P photostimulation with single-cell resolution in freely moving animals. A lightweight implant (0.7 g) ensures that the animal's behavior is not impeded, allowing for stable, hours-long recordings.

The next phase will expand the system to enable simultaneous dual-region investigation. We will develop a double implant strategy, using the 2P-FENDO with two fibers to concurrently image and photostimulate neuronal ensembles in two distinct but connected brain areas. This advancement will provide direct, causal access to the inter-regional dialogue, such as between the hippocampus and prefrontal cortex, that underlies the pathological persistence of memories in disorders like PTSD.

POSTER 38 presented by:

NAME: Yoel Melul

A Closed-Loop System for Real-Time Calcium Imaging, Neuron Selection, and Targeted Photostimulation in Freely Moving Mice

Melul Steinfeld, Yoel [1], Suárez Baquero, David Esteban [1], Accanto, Nicolò [1]
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The combination of 2-photon (2P) calcium imaging and holographic optogenetics allows for precise, minimally invasive recording and manipulation of neuronal activity with single-cell resolution.

We have recently developed 2P-FENDO, a unique platform capable of 2P imaging and photostimulating hundreds of individually selected neurons at single-cell resolution in freely moving mice. It uses a multi-core optical fiber to allow unrestricted movement of the animal, and a spatial light modulator (SLM) to generate dynamic holographic patterns that enable precise control over which neurons are stimulated and when. With 2P-FENDO we can now precisely probe the links between specific patterns of neuronal activity and behavior.

To this end we are developing a real-time closed-loop framework that will: (1) image the activity of thousands of neurons during behavior, (2) computationally identify neural populations whose activity correlates with specific behavioral states or events, (3) photostimulate selected neurons in structured spatiotemporal patterns, and (4) iterate this loop dynamically throughout the experiment.

This framework enables direct testing of the causal role of specific neural ensembles in behavior within a single session. It also opens new opportunities for studying learning, memory, and neuropsychiatric models. In the long term, this platform could support the development and testing of optical strategies for modulating dysfunctional neural circuits in neurological and psychiatric conditions.

We believe that, with this addition, 2P-FENDO will become the tool of choice for neuroscientists to track neuronal circuits and their relation to behaviour in mice.

POSTER 39 presented by:

NAME: Hamed Karami

Smart Sensing and Signal Processing Techniques for Early Detection of Oxidation in Extra Virgin Olive Oil

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The widespread issue of oxidation in Extra Virgin Olive Oil (EVOO) presents significant health risks and quality degradation, impacting both consumers and producers. This study addresses EVOO freshness assessment via a smart electronic nose (E-nose) system, integrating advanced signal processing and machine learning techniques. A multi-gas sensor array, built on the Aryballe NeOse Advance platform, collected volatile organic compound (VOC) profiles from fresh and oxidized oil samples. After pre-processing (including baseline correction, normalization, and smoothing), key features—such as maximum sensor response, area under the curve, and recovery time—were extracted. Multiple classifiers (PCA, PLS-DA, LDA, SVM) were evaluated, with Support Vector Machine (SVM) achieving >94% accuracy. Compared to traditional analytical methods, this approach enables rapid, non-destructive, and cost-effective on-site EVOO freshness evaluation, showcasing the potential of sensor technology and data analytics to monitor quality and ensure product integrity.

POSTER

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POSTER 40 presented by:

NAME: Hamed Karami

Rapid Assessment of Coffee Aroma Profiles Using Multi-Sensor Arrays and Supervised Learning Models

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Volatile compounds play a crucial role in coffee's sensory quality and are significantly influenced by physical processes such as grinding. This study investigated the effect of three grinding degrees (whole bean, medium grind, and fine grind) on the volatile profiles of four commercial coffee types. A gas sensor system (electronic nose) was used to collect and analyze volatile organic compound (VOC) patterns. The data were processed and classified using multivariate techniques, including Principal Component Analysis (PCA), Partial Least Squares Discriminant Analysis (PLS-DA), and Support Vector Machine (SVM).

The results showed a clear and consistent distinction between whole beans and ground samples, while the difference between medium and fine ground coffees was minimal. This differentiation is attributed to the significantly lower surface area exposure in whole beans, which better preserves internal volatiles by limiting oxidation and evaporation. In contrast, grinding increases surface area, accelerating volatile release and chemical transformations. However, once the beans are ground, the additional surface increase between medium and fine grind appears insufficient to cause major further VOC loss, leading to overlapping profiles.

PLS-DA and SVM models both achieved high classification accuracy, with SVM slightly outperforming others, confirming the robustness of pattern recognition for distinguishing whole-bean samples. These findings emphasize the importance of grinding degree on aroma retention and provide a scientific basis for optimizing coffee processing and quality control.

POSTER 41 presented by:

NAME: Mohamed Aziz Ouhida Ben Romdhane

Wasserstein GAN-Based Data Augmentation for Urine GC-IMS Chromatograms

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Gas Chromatography—Ion Mobility Spectrometry (GC-IMS) is being increasingly used in clinical diagnostics due to its ability to rapidly and non-invasively analyse volatile organic compounds such as urine. However, the application of machine learning to GC-IMS data faces critical challenges: the number of labelled samples is often extremely limited, datasets are typically imbalanced across clinical classes, and a significant batch effect exists due to differences in sample origin and instrumental variation. To overcome these limitations and improve generalization and robustness across patient cohorts, data augmentation has become an essential strategy.

In this work, we propose a data-driven augmentation strategy using Wasserstein Generative Adversarial Networks (WGANs). The dataset consists of 2D chromatograms derived from urine samples analysed via GC-IMS, from which we extract chromatograms affected by scarcity, class imbalance, and strong batch effects due to machine variability. The proposed WGAN architecture is designed to generate high-fidelity synthetic chromatograms that mimic the structural and statistical properties of real clinical data.

We systematically evaluate both the realism and utility of the generated synthetic chromatograms. First, we validate that the synthetic samples visually and statistically resemble real chromatograms. Next, we assess their impact on downstream tasks by augmenting small real datasets and measuring improvements in classification performance. To address the critical question of how much real data is needed to train an effective WGAN, we conduct a parametric study: we train WGANs on progressively larger subsets of real samples, enhanced via classical data augmentation (e.g., intensity modulation, time warping), and evaluate the resulting synthetic data quality.

Our results demonstrate that WGANs can generate structurally coherent and class-representative chromatograms even when trained on relatively small datasets, provided that classical augmentation is used to bootstrap variability. These synthetic samples contribute positively to the model's generalization and help counteract dataset imbalance and instrument-origin bias. This work highlights the potential of generative modelling to address core limitations in GC-IMS-based machine learning, paving the way for scalable augmentation frameworks in clinical metabolomics.

POSTER | ICT FOR HEALTH

POSTER 42 presented by:

NAME: Tecla Duran

Removing Systematic Variability from GC-IMS Measurements with Orthogonal Projections

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Gas Chromatography coupled with Ion Mobility Spectrometry (GC-IMS) has become an increasingly valuable tool for untargeted metabolomic fingerprinting, particularly in the analysis of complex biofluids such as urine. However, the reliability of GC-IMS data can be compromised by technical variability arising from experimental conditions during acquisition. This variability can obscure true biological signals, reduce data interpretability, and impair the reproducibility of results.

In this study, we evaluated the impact of acquisition-related variability in a dataset comprising 135 GC-IMS measurements of pooled human urine, distributed across nine consecutive experimental sessions. All samples originated from a common urine pool derived from eleven healthy fasting volunteers and were processed under standardized conditions to isolate the effects of technical drift. The samples were prepared with the addition of sodium chloride, hydrochloric acid, and a ketone internal standard, and measured using an automated injection protocol under fixed incubation conditions.

Two external variables emerged as principal contributors to signal instability: the batch, corresponding to the measurement session, and the elapsed time within each session, representing the time a vial remained at room temperature before analysis. These variables capture, respectively, inter-batch and intra-batch sources of technical variation. Independent linear models fitted to each compound's intensity revealed that around a 35% of the total variance could be attributed to batch effects, and another 35% to elapsed time, suggesting a substantial linear association between acquisition order and signal variability.

To mitigate these effects, we implemented a correction strategy based on orthogonal projections. For each compound, the vector of intensities across all samples was projected onto the subspace orthogonal to the one spanned by selected external variables, removing the component of the signal that can be explained as a linear combination of those covariates. By construction, the corrected signal is uncorrelated with the technical factors used in the model, effectively reducing their contribution to the observed variability.

After correction, the fraction of stable features (defined as those with RSD < 20%) increased from 23% to 71%, indicating a substantial gain in technical reproducibility. Furthermore, simulation experiments mimicking biomarker shifts confirmed an improvement in classification performance, with an average AUC increase of 0.12 for moderate signal perturbations.

POSTER 43 presented by:

NAME: Elena Sossich

Peptide-Based Biosensor for Early Detection of Multiple Sclerosis via Activated VLA-4⁺ Cells

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Multiple sclerosis (MS) is a chronic autoimmune disorder characterized by the infiltration of immune cells into the central nervous system, where they mediate neuroinflammation and demyelination. A hallmark of this process is the expression of the α4β1 integrin, also known as Very Late Antigen-4 (VLA-4), in its activated conformation on the surface of T lymphocytes. These VLA-4⁺ cells, absent or inactive in the cerebrospinal fluid (CSF) of healthy individuals, are significantly overexpressed in the CSF cells of MS patients, making them a promising cellular biomarker for diagnosis. To exploit this specificity, we propose a peptide-based biosensor capable of selectively detecting cells expressing activated VLA-4 in CSF samples.

The biosensor is based on a gold surface coated with antifouling polymer brushes that minimize nonspecific interactions with CSF components, thus improving selectivity and suppressing background signals. The receptor consists of the peptidomimetic ligand BIO1211, which is covalently anchored to the antifouling brushes. Derived from the natural ligand of VLA-4, BIO1211 shows high affinity and specificity for the integrin's activated conformation.

The formation of the antifouling layer and the successful immobilization of the peptide are monitored through a combination of surface characterization techniques. Specifically, Surface Plasmon Resonance (SPR) is used to monitor binding events, ellipsometry to measure film thickness, and X-ray Photoelectron Spectroscopy (XPS) to confirm surface chemistry and validate each modification step.

Following functionalization, the biosensor's ability to selectively capture VLA-4⁺ cells will be assessed using optical microscopy, enabling direct visualization of adherent cells on the sensor surface. To validate the specificity of this interaction, Jurkat cells, known to express VLA-4 in its active conformation, will be employed as a positive control, while HEK cells, which lack VLA-4 expression, will serve as a negative control to evaluate potential nonspecific adhesion.

The final validation step will involve testing the biosensor with clinical CSF samples from both healthy individuals and MS patients, to evaluate its diagnostic performance and real-world applicability.

Due to its high specificity for activated VLA-4⁺ cells in CSF, the biosensor could pave the way for earlier diagnosis of multiple sclerosis, potentially improving patient prognosis and therapeutic outcomes.

POSTER ICT FOR HEALTH

POSTER 44 presented by:

NAME: Gergo Matajsz

13C metabolic imaging methods development for chorioallantoic membrane (CAM) assays

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The chorioallantoic membrane (CAM) assay is a versatile biological model for cancer studies. The fast angiogenesis of chicken embryos provides an optimal, borderline in-vivo physiological environment for tumour growth, achieving sizes comparable to 3–6-week-old mouse models within days [1]. Therefore, they provide a low-cost, high-turnover alternative for studies on real-time cancer metabolism via Hyperpolarized Magnetic Resonance Spectroscopic Imaging (HP-MRSI). Nevertheless, hardware specifically designed for rodents in preclinical MRI scanners (e.g., radiofrequency (RF) coils, positioning bed) needs to be optimized for CAM assays.

We identified and tackled the following challenges in combining metabolic imaging by HP-MRSI with CAM assays:

1. Positioning: We encountered shimming challenges during HP-MRSI studies following ex-situ 1-13C pyruvic acid injection in CAM assays. This occurred due to the eggs' shape and the movement of the chicken embryos, as: a) they hindered the consistent post-injection positioning of our sample with respect to the MRI's B0 field, and b) facilitated the tilting of the RF surface coil due to twisted coaxial cables. We used single pulse 1H sequences with slice selection on unfertilized chicken eggs to troubleshoot this obstacle. With a custom 3D printed holder design we achieved a similar signal-to-noise ratio (SNR) to high-intensity volume coil scans.

2. Cannulations: To avoid shimming disturbances, we explored 3 injection strategies: 1) using 27G stainless steel needles for ex-situ direct tumour injections, 2) PEEK needles in-situ, keeping CAM assays inside the homogeneous B1 field, and 3) 30G stainless steel cannulas in-situ. With cannulations, we observed pyruvate to lactate conversion, a characteristic of the Warburg effect in cancer metabolism. Due to the low SNR of these acquisitions, we need further optimisation in our acquisition strategy.

3. Low SNR: SNR may further be improved by reducing the distance between the receiver loop and our sample, increasing the filling factor arising from their size difference. We propose an adjustable surface coil design descending into the CAM's window.

In this study we troubleshooted issues arising from using CAM assays during MRI experiments with instrumentation designed for rodents. We will investigate the proposed coil design during 13C metabolic imaging experiments to determine the robustness of CAM assays for HP-MRSI.

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POSTER 45 presented by:

NAME: David Gomez-Cabeza

A probabilistic study to uncover biological systems' properties via hyperpolarised nuclear magnetic resonance

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Aims

Hyperpolarised NMR is used to investigate altered metabolic pathways related to diseases. Yet, it is scarcely used to better understand the systems involved, resulting in potential non-biologically assumptions on kinetics. Here, we use mathematical models and Bayesian statistics to elucidate the mechanisms of pyruvate to lactate conversion *in vivo* and propose an experimental design approach to minimise experimental time and costs.

Methods

We used HepG2 cell suspensions and added hyperpolarised [1-13C]pyruvate (0.1-40 mM). We measured all samples with a benchtop NMR. We developed all ordinary differential equations using mass action kinetics. All code was developed with Julia programming. We used Stan for all Bayesian inferences (BI). For the in-silico study of Bayesian optimal experimental design (bOED) we maximised the posterior prediction uncertainty.

Results

For simpler models, we proved that kinetic rates are a product of the average single-cell rates by the total cell number. Fitting a basic linear model to the three datasets resulted in suboptimal predictions. We expanded the model to include pyruvate internalisation by MCT transporters, providing significantly better posterior predictions with a single set of parameter posteriors. Yet, model predictions are incapable to recapitulate the general system's behaviour, showing inhibition at high [pyruvate], requiring more complex models. Increase in model complexity negatively affects the time needed for inferences and simulations. We also computationally validated a novel approach for bOED. The results spotlighting OED as the best option to reduce experimental and computational time and costs.

Conclusions

We systematically employed mathematical modelling and Bayesian inference to better understand core biological systems of high importance in cancer studies in HP-NMR. Furthermore, we validated a novel approach for bOED to reduce computational and experimental time and resources when deriving complex models.

POSTER | ICT FOR HEALTH

POSTER 46 presented by:

NAME: Martín Ruiz Gutiérrez

Surface plasmon resonance sensing platform for real-time fibrosis monitoring of Duchenne Muscular Dystrophy organ-on-a-chip model

Martín Ruiz-Gutiérrez [1], Chiara Ninfali [1], Mehdi Torabi-Goodarzi [1], Elia López-Serrano [1], Esther Fernández-Simón [2], Jordi Díaz-Manera [2], Javier Ramón-Azcón [1,3], Juan M. Fernández Costa [1]

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Muscular dystrophies encompass a wide range of debilitating diseases characterized by progressive muscle weakness and atrophy. In affected individuals, skeletal muscles undergo progressive loss of muscle fibers, replaced by fibrotic tissue that prevents muscle regeneration and limits the response to therapeutic interventions. Here, we present an innovative approach to monitor fibrosis *in vitro* using 3D cultures of fibro/adipogenic progenitor cells (FAPs) coupled with optical sensors. Initially, we characterized collagen accumulation in 3D FAP cultures derived from Duchenne Muscular Dystrophy (DMD). While conventional methods like ELISA and soluble collagen assays (SIRCOL) did not detect increased collagen-I in the culture supernatants, we identified a significant increase of the N-terminal propeptide of type 1 collagen (PINP), a marker of collagen-I fiber formation. To monitor fibrosis progression, we developed a plasmonic sensor specifically targeting PINP. This surface plasmon resonance-based optical sensor enables label-free, real-time detection of the peptide. Integration of this platform involved incorporating FAP 3D cultures into a microfluidic organ-on-chip device linked to nanoplasmonic biosensors for PINP detection. We confirmed the increase in fibrosis levels in DMD compared to healthy control tissues through PINP quantification. Fibrosis levels of control and dexamethasone-treated samples were compared to assess the effectiveness of this antifibrotic drug on our model as a means of validation of the drug testing capabilities of our platform. This biosensing platform facilitates the continuous monitoring of collagen synthesis by FAPs, offering a valuable tool for screening potential anti-fibrotic therapies and new treatments for muscular dystrophies.

POSTER 47 presented by:

NAME: Petra Bauzon

Biosensing in complex media: development of an anti-fouling biofunctionalization strategy for plasmonic biosensors.

Bauzon, Petra [1], Torabi Goodarzi, Mehdi [1], Kasapgil, Esra [2], Rodriguez-Emmenegger, Cesar [2], Ramón Azcón, Javier [1]

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Surface plasmon resonance (SPR) biosensors are powerful tools in diagnostics, and continuous work is done to increase their sensitivity, enabling the detection of extremely low concentration of molecules. However, real-life detection of analytes should be performed mostly in complex media, where many other species are present. Such species can adsorb on the surface of the sensor, phenomenon called fouling, causing a non-specific signal component. Therefore, is important to develop anti-fouling biofunctionalization strategies to inhibit the non-specific adsorption of proteins, allowing reliable and specific biomarker detection. Here, we assessed two surface biofunctionalization strategies to identify the best one in terms of anti-fouling properties. By using real-time measurement of plasmonic biosensors, we demonstrated that simply obtainable surface-attached hydrogel coatings possess excellent resistance to non-specific adsorption, both with single-protein systems and complex systems. No detectable adsorption was found after BSA, fibrinogen and culture medium injections in the system. Moreover, such coating did not have a high impact on the bulk sensitivity of the biosensor. Some preliminary tests with human serum, suggest the potential optimization of such anti-fouling strategy for highly complex media. The next step will be the identification of a simple, yet effective technique to allow antibody immobilization on the hydrogel coating. Achieving a surface biofunctionalization that combines outstanding anti-fouling capabilities with selective analyte-capturing abilities would enable to obtain a specific and reliable biosensor for detection in complex media. Moreover, such biosensor has high versatility to be employed in a plethora of applications, tailoring it to the needs by changing the bioreceptor employed.

POSTER

ICT FOR HEALTH

POSTER 48 presented by:

NAME: Daniel Romero

Feasibility of cellulose-based electrodes for ECG parameter analysis: preliminary assessment in healthy volunteers

Daniel Romero Pérez [1], Aleix Martí Maymó [2], Antón Guimerà Brunet [2], Mahtab Mohammadpoor Faskhodi [1], Yolanda Castillo Escario [1], Fabiola Vilaseca Morera [3], Gemma Gabriel Buguña [2], Raimon Jané Campos [1]

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The increased demand for sustainable biomedical devices has motivated the use of novel substrates for electrophysiological monitoring. Cellulose, a biodegradable and low-cost material, offers an attractive alternative to conventional electrodes. This study presents a preliminary evaluation of cellulose-based electrodes for electrocardiography (ECG) acquisition under resting conditions. Acknowledgments: This study was supported by the Departament de Recerca i Universitats; del Departament d'Acció Climàtica, Alimentació i Agenda Rural; i del Fons Climàtic de la Generalitat de Catalunya for the project “Green Electrodes for Sustainable Electrophysiology” (2023 CLIMA 00075).

The proposed electrode consists of a three-layer architecture: a conductive vegetal cellulose film doped with PEDOT:PSS (50:50 weight ratio) as the core, an adhesive layer, and a hydrogel layer, assembled by rapid prototyping. Its rectangular geometry (2.5 × 2 cm, with a 1 cm connection tab) balances conductivity and mechanical flexibility. ECG signals were simultaneously recorded from cellulose-based and standard reference electrodes placed in bipolar lead I (see Fig. 1) in three healthy volunteers (mean age 25 ± 10 years). Recordings lasted ~150 s at a 1000 Hz sampling rate. Preprocessing included baseline drift attenuation and fourth-order Butterworth low-pass filtering (45 Hz), followed by automatic QRS detection and delineation. Morphological similarity was assessed using Pearson’s correlation coefficient (r) and Root Mean Square Error (RMSE). Frequency-domain analysis was performed through power spectral density (PSD, Welch’s method) and coherence analysis. Cardiac intervals of clinical relevance including the RR interval (RR), QRS duration (QRSd), QT interval (QT), and Tpeak-to-Tend (Tpe), were estimated from delineated signals.

Results showed strong agreement between electrodes ($r = 0.87 \pm 0.09$; RMSE = 0.10 ± 0.03). Reference signals displayed slightly higher power at low frequencies (<10 Hz), consistent with coherence findings. Interval analysis revealed minimal errors for RR and QRSd, while QT and Tpe presented larger deviations, likely due to challenges in T-wave end delineation. These findings support the feasibility of cellulose-based electrodes as a sustainable and reliable alternative for ECG monitoring, with further optimization required to improve T-wave interval estimation.

POSTER | ICT FOR HEALTH

POSTER 49 presented by:

NAME: Manuel Lozano

Performance Evaluation of Tattoo Skin Electrodes for Measuring Respiratory Muscle Activity in Healthy Subjects

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Measuring respiratory muscle activity is essential for assessing chronic respiratory diseases and neuromuscular disorders, and can be noninvasively performed by surface electromyography (sEMG) over lower intercostal spaces [1]. The use of commercial wired Ag/AgCl electrodes and complex acquisition setups has limited the application of sEMG to laboratory and clinical settings. Tattoo skin electrodes are currently emerging as a new wearable technology to measure electrophysiological signals [2]. This study aims to evaluate the performance of tattoo skin electrodes for measuring respiratory muscle activity over lower intercostal spaces.

In-lab tests were performed in 6 healthy participants (2 males, 36 (25-46) yrs., 23.5 (18.9-26.5) kg/m2), using 2 tattoo sensors for recording 4 lower right intercostal space sEMG signals (inter-electrode distances of 1.35, 2, 2.7, and 4.05 cm), during quiet and deep breathing, a Valsalva manoeuvre, and coughing. Reference measurements were obtained with commercial Ag/AgCl electrodes (Kendall H124SG, 2.4 cm diameter) and a respiratory band signal (TSD201, BIOPAC). All signals were acquired at 2000 Hz (MP150, BIOPAC). sEMG signals were converted to fixed sample entropy (fSampEn), as in [3], and compared with respiratory band signals using maximum cross-covariance (cMAX). For each sEMG signal, 4 respiratory muscle activity measures were obtained by averaging mean inspiratory fSampEn values of quiet breathing, deep breathing, Valsalva, and coughing segments. Agreement between tattoo and Ag/AgCl measures was assessed using Pearson's and intra-class (ICC2,1) correlation coefficients.

Similar cMAX values were provided by tattoo (0.727) and Ag/AgCl (0.716) electrodes, representing moderate-to-strong relationships between fSampEn and respiratory band signals. Very strong correlations (0.858-0.931) and good-to-excellent agreement (ICC2,1 = 0.759-0.919) were obtained between tattoo and Ag/AgCl measures (Fig. 1). Since greater inter-electrode distances result in greater sEMG amplitudes, tattoo inter-electrode distances shorter (1.35 and 2 cm) and larger (2.7 and 4.05 cm) than that of reference electrodes (2.4 cm) yielded systematically lower and higher measures, respectively.

Tattoo sensors are a promising alternative to commercial Ag/AgCl electrodes for measuring respiratory muscle activity, being more comfortable for patients, allowing easy design of electrode arrays for multichannel recordings, and representing an advance towards continuous and remote monitoring of patients with respiratory muscle weakness in real-world settings.

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POSTER ICT FOR HEALTH

POSTER 50 presented by:

NAME: Yolanda Castillo

Assessment of Sleep Apnea in Stroke Patients using Smartphone Technology

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Sleep apnea is common but often underdiagnosed after stroke, hindering rehabilitation and functional recovery. Access to sleep studies remains limited for stroke patients, partly due to the inconvenience of current diagnostic tools. The widespread availability and built-in sensors of smartphones make them powerful solutions for mobile health applications, including sleep monitoring. This study aims to detect and evaluate sleep apnea in post-stroke patients using a smartphone and extract multimodal digital biomarkers to characterize their sleep patterns. For that, overnight sleep tests were conducted on 30 subacute stroke patients and 30 age- and sex-matched control subjects, using a smartphone-based system that recorded audio, accelerometer, and oximetry data. Signals were analyzed with custom-made algorithms to compute respiratory, oxygenation, and sleep position indices. Results showed that the apnea-hypopnea index (AHI) was significantly higher in the stroke than the control group (28±19 vs 14±11, p=0.006). Moderate-to-severe sleep apnea (AHI≥15) was present in 67% of stroke patients and 40% of control subjects. Stroke patients spent more time mouth breathing (22% vs 12%, p<0.001) and sleeping in supine position (67% vs 35%, p<0.001) than controls, contributing to upper airway obstruction. These findings obtained with novel multimodal digital biomarkers improve the understanding of post-stroke sleep apnea patterns and show the potential of smartphones as portable monitoring tools. This approach can facilitate early sleep apnea detection after stroke, thereby reducing its substantial burden and improving rehabilitation outcomes.

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FLASH PRESENTATION | MECHANOBIOLOGY

FLASH 51 presented by:

NAME: Thomas Wilson Thomas Wilson

Engineering epithelial cell shape and mechanics to create a new generation of biohybrid devices

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All surfaces of our body, both internal and external, are covered by thin cellular layers called epithelia. Epithelia are responsible for fundamental physiological functions such as morphogenesis, compartmentalization, filtration, transport, environmental sensing, and protection against pathogens. These functions are determined by the three-dimensional (3D) shape and mechanics of epithelia. One commonly formed shape are 3D tubular structures, such as blood vessels, lung bronchioles, and kidney renal tubules. However, the mechanisms behind how epithelial tubes behave under differing flows and geometric conditions remains poorly understood. We aim to address this question by developing a technology to engineer the elementary building blocks of epithelial morphogenesis and to reverse-engineer their mechanics. With a combination of micropatterning, sacrificial matrices, and microfluidics, we will implement a new experimental platform to sculpt epithelial tubes of a controlled geometry. We apply these engineering principles to build biohybrid devices based on 3D epithelia and create a microfluidic channel composed of epithelial tissue that can be imaged with high spatial-temporal resolution. Through this approach, we will map the stress and strain tensors and luminal pressure, and then to control these variables from the subcellular to the tissue levels. We aim to perform full experimental study of the 3D mechanics of tubular epithelial channels, and to unveil the mechanical principles and underlying forces by which these tissues adopt and sustain their shape. Our study establishes a new approach for engineering epithelial biohybrid microfluidic devices.

FLASH 52 presented by:

NAME: Juan Francisco Abenza Martínez

The mechanical control of the mammalian circadian clock

Juan F. Abenza [1], Leone Rossetti [1], Malèke Mouelhi [1], Stijn van der Klei [1], Javier Burgués [1], Ion Andreu [1], Keith Kennedy [3], Pere Roca-Cusachs [1, 4], Santiago Marco [1, 5], Jordi García-Ojalvo [3], and Xavier Trepat [1, 2, 4, 6]

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Cells sense and respond to the mechanical properties of their environment through diverse pathways that impact gene expression and affect key processes such as migration, proliferation, and differentiation. Recently, mechanics has also been shown to influence circadian rhythms, broadening its importance in tissue homeostasis. This project aims to understand how the circadian clock in individual mammalian cells is influenced by their physical context.

We used a transcriptional fluorescent reporter of the circadian clock gene Rev-erbα (RevVNP), confocal microscopy, computational analysis, and microfabrication to study the clock in different mammalian cell types. In a first phase, using NIH3T3 mouse fibroblasts, we observed that basal and circadian RevVNP expression—typically low and rhythmic in dense, jammed monolayers—is perturbed at low density, when cells are allowed to freely migrate.

We then confined single cells in islands of different sizes using fibronectin micropatterning. As in dense monolayers, we found that the robustness of RevVNP circadian oscillations in isolated cells correlated with the level of confinement. By examining the intracellular localisation of the mechanosensitive transcriptional regulators YAP/TAZ under a series of mechanical perturbations, we observed a strong anticorrelation between RevVNP circadian robustness and YAP/TAZ nuclear levels. Overexpression of YAP/TAZ severely impaired the oscillations of the main core clock transcripts (Bmal1, Rev-erbα, and Cry1), which demonstrates a direct role for YAP/TAZ as circadian modulators.

Given the broad importance of YAP/TAZ as mechanoregulators, our next goal is to determine whether they can also regulate the clock in more complex tissues, like the small intestinal epithelium. This tissue is highly subjected to mechanical forces and its activity is regulated by the circadian clock.

We have developed and characterised new fluorescent reporters to track Bmal1 expression in individual cells within mouse intestinal organoids grown in 2D. Our preliminary results indicate that YAP/TAZ levels—high in the stem cell niche and low in differentiated enterocytes—correlate with both Bmal1 and Rev-erbα basal expression. Although both stem cells and enterocytes display robust Bmal1 oscillations, we have found intriguing differences in phase and amplitude. This reflects complex regulation based on distinct time interpretations by the different cell types that compose the intestinal epithelium.

FLASH PRESENTATION | MECHANOBIOLOGY

FLASH 53 presented by:

NAME: Marina Placci

Nanomechanical traits for Rare Diseases: spotlight on Gaucher and Fabry diseases

Placci, Marina [1,2,3], Valotteau, Claire [4], Redondo-Morata, Lorena [4], Casasampere Ferrer, Mireia [5], Muro, Silvia [2,6], Giannotti, Marina Inés [1,7,8]

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Gaucher disease (GD) and Fabry disease (FD) are systemic, progressive, and often underdiagnosed rare lysosomal storage disorders (LSDs). Caused by mutations in lysosomal enzymes, they lead to pathological lipid accumulation. In GD, β-glucosidase deficiency causes glucosylceramide (GlcCer) buildup, while in FD, deficient α-galactosidase activity results in globotriaosylceramide (Gb3) accumulation. These lipid storage defects result in a wide range of clinical manifestations—from organ dysfunction to neurological involvement—and may ultimately lead to patient death. While their genetic and biochemical bases are well studied, the impact of lipid accumulation on membrane structure and nanomechanics remains poorly understood.

In this study, we combined cellular lipidomics with biophysical assays to explore how GlcCer and Gb3 affect membrane architecture and mechanics, key elements in cell signaling and function. First, lipidomic profiles of fibroblasts from GD and FD patients were compared to healthy controls, revealing distinct alterations upon metabolic stimulation with sphingosine (5 μM, 24 h).

To model the membrane-level effects of lipid accumulation, supported lipid bilayers (SLBs) were engineered using physiologically relevant lipids (Dioleoyl-phosphocholine (DOPC), sphingomyelin, and cholesterol) with or without GlcCer or Gb3. AFM and AFM-based force spectroscopy were used to characterize membrane topography and mechanical properties, where the breakthrough force (Fb) was determined as an indicator of lipid lateral interactions and membrane rigidity.

We found that both GlcCer and Gb3 segregate into domains within simple DOPC membranes. In more complex SLBs, GlcCer increased domain rigidity and packing, whereas Gb3 disrupted phase organization, leading to phase inversion, highlighting distinct nanomechanical fingerprints for each disease-associated lipid.

Finally, we extended these findings to living cells: these membrane-level effects were correlated with whole-cell nanomechanics in fibroblasts from GD and FD patients. Together, our results highlight how lysosomal lipid accumulation can influence membrane and cell nanomechanics —revealing nanomechanical traits linked to disease pathogenesis and supporting the development of more targeted, precision medicine strategies in LSDs.

FLASH 54 presented by:

NAME: Beatriz Cantero Nieto

Highthroughput biomechanical characterization of macrophage polarization through atomic force microscopy

Beatriz Cantero Nieto [1, 2], Mauricio Cano Galván [1,2], Gabriel Gomila Lluch [1, 2], Annalisa Calò [1, 2],
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Macrophages play a critical role in innate immunity and are involved in a wide range of biological functions. Due to high plasticity, macrophages can be polarized into different phenotypes depending on the microenvironment, enabling them to perform specific functions during inflammation. This polarization capability underscores the importance of identifying biomechanical differences between various macrophage subtypes, as these variations could serve as valuable indicators for early diagnosis in various diseases Including chronic inflammatory diseases (such as rheumatoid arthritis, fibrosis, and atherosclerosis), neurodegenerative diseases, and cancer [1].

However, neither standardized measurement protocol or robust biomechanical analysis currently exists to efficiently explore these differences. In this context, atomic force microscopy (AFM) has emerged as an ideal tool, as it allows mapping cellular biomechanical properties with high spatial resolution under physiological conditions. To enable precise identification and differentiation of these phenotypes, we present a measurement protocol in which key experimental parameters are carefully controlled, along with the development of accurate analytical models and advanced data analysis techniques integrated with artificial intelligence. These results open new avenues for macrophage research and, more broadly, for highthroughput cell nanomechanical studies, projecting the AFM technique into real clinical applications.

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POSTER MECHANOBIOLOGY

POSTER 55 presented by:

NAME: Mauricio Cano Galván

Mechanotool: Towards an Autonomous Open-Source Software Platform for Large-Scale Mechanical Analysis of Bio-Atomic Force Microscopy data

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Atomic Force Microscopy (AFM) enables high-resolution mechanical characterization of biological samples at the nanoscale, but the vast amount of data it generates often remains underutilized due to the lack of automatized, scalable, and flexible nanomechanical AFM analysis software tools. Mechanotool has the aim to address this challenge by providing an open-source Python-based, modular platform for the automated, high-throughput analysis of AFM force-distance curves and topographical data acquired on biological samples (cells, bacteria, viruses, proteins, etc.). Mechanotool supports the AFM data analysis process from start to finish: from raw curve importation, visualization, and quality assessment to advanced mechanical modeling and topography refinement. It enables in-image photodiode sensitivity calibration, smart segmentation of regions of interest, and includes preprocessing routines comparable to those found in commercial tools. The tool also incorporates customizable fitting models, including those that account for bottom-effect corrections and double-regime behaviors, features that often require manual implementation or in-house software. The platform is also useful for refining topographical maps by using mechanical data to correct for height underestimations caused by tip indentation. This allows for more accurate application of mechanical models, particularly those that incorporate bottom-effect corrections, as height plays a critical role in these calculations. As a result, Mechanotool enables more precise estimation of Young's moduli across entire AFM images. The software's modular design allows for the integration of advanced analysis techniques, such as AI-assisted segmentation or curve filtering, further reducing manual intervention and enhancing experimental reproducibility. This paves the way for more scalable, consistent, and insightful studies of mechanics at the nanoscale, while aiming to provide a more hands-off experience for AFM users.

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POSTER 56 presented by:

NAME: Yogita Maithani

Local conduction properties of cable bacteria fiber sheaths after UV and humidity exposure using scanning dielectric force microscopy

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Cable bacteria (CB) are filamentous microbes capable of long-range electron transfer via protein-based fibers embedded within their periplasmic sheath. Understanding their electrical conduction properties under different environmental conditions is essential to evaluate their bioelectronic functionality [4]. We measured the electrical conduction properties of cable bacteria sheaths after UV light and humidity exposure using microelectrodes and current-voltage (I-V) measurements and scanning dielectric microscopy. The I-V measurements showed the degradation in the electrical conduction of CB after short UV exposure in ambient conditions. However, local electric force measurements showed that locally CB still show some conductivity, which cannot be detected by the microelectrode measurements. After prolonged UV exposure, the electrostatic force is reduced, which indicates that it eventually suppresses even the local conduction of CB.

POSTER | MECHANOBIOLOGY

POSTER 57 presented by:

NAME: Rohit Nautiyal

Role of nematic order in tissue reshaping

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From the earliest stages of development and during life, cells self-organize within tissues by actively coordinating their behavior, guided by chemical and physical cues. In tissues, composed of elongated cells, orientational neumatic order emerges as a crucial cue giving rise to anisotropic mechanics and regulating tissue forces. While previous works with 2D monolayers have elucidated the role of nematic order in the guidance of tissue dynamics and mechanics, their impact on 3D tissue remodelling remains largely unexplored. To address this gap, we investigate the three-dimensional stretching and compression of nematically ordered monolayers using a monolayer inflation system. We employ brain endothelial (bEnd3) cells, which form nematically aligned cohesive monolayers exerting forces guided by local disordered regions that condigured topological defects of orientation. To control nematic order, we use anisotropic micropatterns of adhesions, which enables to control cell alignment. Our results show that bEnd3 cells align and mature successfully on micropatterns and forms stable nematic monolayer with controlled alignment. By integrating guided alignment with the monolayer inflation platform, we are exploring how predefined cellular orientation influences tissue stretching upon inflation and guides tissue folding during deflation. By doing this, we aim to understand the role of nematic alignment in shaping tissues, offering new insights into developmental biology and tissue engineering.

POSTER 58 presented by:

NAME: Janet van der Graaf Mas

Experimental model of the mechanobiology of the immunocompetent tumor ecosystem

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The progression of a tumor and its response to therapy depend on the evolution of a complex tumor microenvironment (TME) that includes cancer cells, cancer-associated fibroblasts (CAFs), endothelial cells and immune cells, among others. In many types of solid tumors, the TME prevents immune cells from eliminating the disease by inhibiting their capacity to migrate into the tumor, which typically leads to immunotherapy failure. Growing evidence shows that the main contributors to immune exclusion are CAFs, who envelop the tumor and exert active compression on cancer cells. This physical barrier, together with the secreted signaling proteins and ECM components create a barrier to immune infiltration. To understand how mechanochemical interactions drive tumor progression and how they determine treatment efficacy, there is a need to develop experimental models of the tumor ecosystem. Here we present the proof-of-concept of our technology, which we call Tumor Ecosystem On Chip (TEOC), a microphysiological system that enables control and measurement of the mechanobiology of the TME, focusing on immune exclusion. By using surface micropatterning, we are able to control cell alignment and investigate the effects of CAFs architecture and mechanobiology on immune cell migration. This will allow us to investigate by which mechanisms the spatial alignment of CAFs and the mechanobiological properties of the TME determine immune infiltration.

POSTER MECHANOBIOLOGY

POSTER 59 presented by:

NAME: Alice Perucca

Fibroblast nematicity as a tool to study stromal control on immune migration.

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The tumour microenvironment (TME) is a complex system composed of cancer cells, immune cells, cancer-associated fibroblasts (CAFs), and an extracellular matrix (ECM) whose structural organization critically influences tumour progression. A hallmark of the TME is the CAF-driven alignment of ECM fibers, especially fibronectin, which displays characteristics of nematic ordering, a concept from liquid crystal physics describing the collective orientation of elongated entities. Disruptions in this order, known as nematic defects, emerge where local orientations mismatch. These features have been shown to appear near the interface between tumour and surrounding stroma. Here, nematic defects are proposed to play a role in cell motility, immune exclusion, and mechanical stress propagation. CAFs and the ECM often mirror each other in alignment and defect patterns, suggesting a feedback between cellular organization and matrix structure.

Building on these findings, we examine how nematic ordering and defects within CAF monolayers affect T cell behaviour. Using a controlled *in vitro* system, fibroblast monolayers cultured on polyacrylamide gels and overlaid with a 3D-confining agarose pad, we investigate how T cells migrate across aligned versus disordered fibroblast networks. Since immune cells can follow aligned fibers and dense ECM impedes their infiltration, we explore how nematic alignment and its defects may serve as physical cues or barriers to immune cell access. This work aims to elucidate the biological significance of nematic organization in cancer, particularly in the context of immune cell migration and immune exclusion.

POSTER 60 presented by:

NAME: Mireia Valero Puigdomenech

Macrophage polarization in viscoelastic environments

Valero Puigdomenech, Mireia [1], Azevedo Gonzalez Oliva, Mariana [1], Salmeron-Sanchez, Manuel [1]
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Tissues are viscoelastic materials, and their mechanical properties evolve over time, influencing processes such as tissue repair and regeneration. Macrophages, immune system cells derived from bone marrow monocytes, are key to these processes and perform multiple functions including phagocytosis, immunomodulation and coordination of tissue remodeling. Their high plasticity allows them to adopt different phenotypes, ranging from pro-inflammatory to anti-inflammatory or pro-regenerative, in response to environmental cues. They also maintain dynamic interactions with bone marrow mesenchymal stem cells (MSCs), which have immunomodulatory effects, and their fate and function are influenced by macrophage phenotype. While the impact of substrate elasticity on macrophages behavior has been established, there is limited understanding of how extracellular matrix (ECM) viscoelasticity influences these immune cells.

In this project, we investigate how the viscoelastic properties of synthetic ECM influence macrophage polarization and their crosstalk with MSCs. To this end, we use polyethylene glycol-maleimide (PEG-MAL) hydrogels with independently tunable elasticity (stiffness) and viscoelasticity (stress relaxation) that can incorporate biological functionalities such as growth factors and cytokines to mimic physiological relevant microenvironments. Human macrophages (derived from monocytes) and MSCs are co-cultured within these matrices, and their behavior and interaction with their surroundings is monitored in real time by using Brillouin microscopy, a non-invasive method for microscale mechanical characterization. This strategy allows a mechanistic understanding of how ECM viscoelasticity influences immune-stem cell interactions, offering insights into regenerative processes and guiding the design of immunomodulatory biomaterials with better biological mimicry and functionality.

POSTER MECHANOBIOLOGY

POSTER 61 presented by:

NAME: Margherita Gallano

Nuclear Envelope Remodeling and Mechanosensing Mechanisms under Stretch

Margherita Gallano [1,2], Aina Albajar Sigalés [1,2] , Evelyn Coderch Bifet [1] , Miguel González Martín [1,2] ,Nimesh Chahare [1,3], Anabel-Lise Le Roux [1], Pere Roca-Cusachs [1,2]
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Mechanical forces drive cell function in multiple scenarios, often via cellular membranes. Under mechanical stimulation, the plasma membrane has been shown to exhibit a wide range of responses, including changes in membrane tension, lipid packing and order, and the rearrangement of membrane folds of different types. These membrane responses affect lipid associated proteins, triggering downstream signaling processes that could also occur in other cellular membranes. The case of the nuclear envelope (NE) is of particular interest, as mechanical forces are transmitted to the cell nucleus. The NE can indeed respond to force, as shown by the activation of NE-binding enzyme cPLA2 in response to NE tension. However, the phenomenology of NE responses to force remains largely unexplored. In this project, we aim to characterize the dynamic response of the NE under stretch or compression and unravel related mechanosensing and downstream signaling. To this end, we use isolated nuclei as a model system, allowing us to directly probe the NE with fluorescent reporters to assess its tension and fluidity, while excluding cytoskeletal contributions. We intend to apply stretch on the isolated nuclei, by employing a custom-designed microfluidic device featuring a stretchable membrane.

POSTER | MECHANOBIOLOGY

POSTER 62 presented by:

NAME: Jorge Oliver-De La Cruz

Stiffness-Regulated Microtubule Stability Controls Tau Phosphorylation and Nuclear Localization in Neurons

Jorge Oliver-De La Cruz [1], Pau Guillamat [1], Paolo Paganetti [2,3], Mar Altadill-Cordero [1], Xavier Trepat [1,4,5], Pere Roca-Cusachs [1,6]
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Brain tissue stiffness changes significantly during development, aging, and in pathological conditions. In neurodegenerative diseases such as Alzheimer's disease (AD), these mechanical alterations occur in parallel with neuronal loss, synaptic dysfunction, and inflammation, but a causal relationship has not been established.

To explore the role of neuronal mechanosensing in AD-related pathology, we developed a model using SH-SY5Y-derived neurons, differentiated through NGN2 overexpression and biochemical induction, and cultured them on laminin-coated polyacrylamide hydrogels spanning different stiffnesses. Neurons on softer substrates showed reduced spreading, shorter neurites, and impaired axonal microtubule networks, as demonstrated by reduced tubulin acetylation. Pharmacological perturbation of the cytoskeleton revealed that microtubules are key determinants of neuronal morphology and mechanotransduction. Importantly, microtubule disruption in soft matrices led to increased phosphorylation of Tau (Thr202/Thr205), a hallmark of AD, which accumulated in the nuclei.

These mechanosensitive effects were recapitulated in human iPSC-derived neurons from an AD patient carrying the APOE4/E4 genotype and an isogenic APOE3/E3 control. APOE4 neurons on soft substrates showed exacerbated AD-related phenotypes, including perinuclear and nuclear accumulation of phosphorylated Tau, suggesting a synergistic interaction between genetic risk and mechanical cues.

Our findings highlight a mechanistic link between brain tissue stiffness, cytoskeletal destabilization, and Tau pathology. This work underscores the importance of mechanical signaling in neuronal health and disease and suggests that targeting mechanotransduction pathways may offer new therapeutic avenues for AD.

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POSTER MECHANOBIOLOGY

POSTER 63 presented by:

NAME: Guillermo Martínez Ara

An optogenetic toolset to understand and control epithelial mechanical balance

Guillermo Martínez Ara [1], Emmanuel Spanoudakis [1], & Xavier Trepat Guixer [1, 2, 3, 4]
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Cells form tissue structures through the interaction of mechanical forces[1]. Synthetic biology proposes the control of such forces to improve our understanding of how tissue structures arise[2]. In addition, optogenetics has opened the possibility of gaining spatio-temporal control of mechanical forces with light[3]. These approaches have proven to be useful for the study of epithelial morphogenesis[4,5]. However, the experimental control achieved doesn't account yet for all the forces proposed in physical models of tissue morphogenesis. Several theoretical studies propose an epithelial mechanical balance between apical, lateral, and basal contractility[6]. In this project, we make use of optogenetic and synthetic approaches to gain control over this set of forces (apical, basal, and lateral contractility) to test whether they are sufficient to understand and control the shape of different epithelial cell types.

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POSTER 64 presented by:

NAME: Aurora Dols Perez

Nanomechanics of long-distance electron conductive multicellular cable bacteria

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Cable bacteria are filamentous multicellular systems that exhibit long-distance electron transport (LDET) in the millimeters or centimeters range [1, 2]. They show a structure of thousands of bacterial cells connected end to end and surrounded by a periplasmic network of ordered fibers. These fibers are suspected to be conductive and responsible for the electron transport, but their composition and physicochemical properties are still unknown.

Cable bacteria are filamentous multicellular systems that exhibit long-distance electron transport (LDET) in the millimeters or centimeters range [1, 2]. They show a structure of thousands of bacterial cells connected end to end and surrounded by a periplasmic network of ordered fibers. These fibers are suspected to be conductive and responsible for the electron transport, but their composition and physicochemical properties are still unknown.

In here Atomic Force Microscopy (AFM) and mechanical imaging have been used to obtain new information about these systems. For this purpose, two different types of samples have been studied, intact cable bacteria and cable bacteria sheaths obtained by a treatment of decellularization with SDS+EDTA. Both samples were studied under two different ambient conditions, dried and after rehydration.

Fibers were observable in dry cable bacteria sheaths but were not evident on intact cells or hydrated samples. In fact, results showed a high dependence on the hydration state of both samples. Both showed a deep change in their dimensions due to swelling after the rehydration and differences in the adhesion and Young's modulus. These results open new insights into the characterization of cable bacteria and provide new information about their unknown structure, relevant for their potential technological applications.

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POSTER 65 presented by:

NAME: Valeria Venturini

Force transmission and mechano-transduction from cell-cell adhesions to the nucleus

Venturini, Valeria [1], Faure, Laura [1], Baguer Colomer, Ona [1], Fläschner, Gotthold [1], Roca-Cusachs, Pere [1]
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Cells sense and respond to mechanical signals from their environment via a process known as mechanotransduction. Among other mechanisms, single cells can sense the stiffness of their extracellular environment (ECM) via direct mechanical coupling of the nucleus via the LINC complex to the actin cortex and via integrin-based adhesions, to the ECM. In stiff environments, the traction force induces nucleus flattening and nuclear envelope stretch that leads to nuclear pore opening. This further regulates nucleo-cytoplasmic transport of mechanosensitive molecules and transcription factors, thereby regulating transcription.

However, how these processes are controlled in cells that are connected to neighbors via cell-cell junctions is not known. To dissect this question, we design *in vitro* minimal systems to specifically address the role of eCadherin-based adhesions in nuclear force transmission and mechanotransduction, using human breast cancer epithelial cells. Preliminary results show that eCadherin binding prevents cell spreading and consequent nucleus flattening by re-organizing the microtubules network, further controlling nucleo-cytoplasmic transport and downstream mechanosensitive pathways.

POSTER 66 presented by:

NAME: Gotthold Fläschner

Nuclear mechanics regulates the organization of FG-nups in nuclear pore complexes

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The application of mechanical tension to the nuclear envelope has been recently shown to dilate nuclear pore complexes (NPCs) and increase their permeability. However, how this relates to the organization of the disordered proteins that regulate NPC permeability, FG nucleoporins (FG nups) is unknown. Further, how different types of mechanical stimulation affect NPCs, and how mechanical effects propagate spatially within nuclei, is also unclear. By using Stochastic Optical Reconstruction Microscopy (STORM) and image analysis algorithms, here we show that mechanical tension applied to the nuclear envelope through osmotic shocks alters the distribution of FG-nups, reducing their density in the central channel. Preliminary data also show that different types of mechanical perturbations (osmotic shocks, changes in substrate stiffness, and actomyosin inhibition) lead to different spatial regulations of FG nups within NPCs, which could be explained by mechanical tension.

POSTER MECHANOBIOLOGY

POSTER 67 presented by:

NAME: Marc Rico Pastó

Shear stress resistance reveals metastatic potential in solid tumor cell lines

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Metastasis is the leading cause of cancer-related death worldwide. Despite this, it remains one of the least understood aspects of cancer biology, mainly due to the difficulty of modeling its complexity *in vitro*. The metastatic cascade is a multi-step process including migration and invasion, intravasation, circulation, extravasation, and colonization. While most of these phases can be reasonably reproduced *in vitro*, modeling the circulation step remains a technically challenging task. At this stage, circulating tumor cells (CTCs) must survive in suspension and endure constant mechanical stress within the bloodstream. Most CTCs die in this hostile environment, but those that survive are the ones with real metastatic potential. How CTCs overcome the pro-apoptotic cues posed by the hydrodynamic conditions within the circulation (shear stress, hydrostatic pressure) remains largely unknown. To address this knowledge gap, we designed a microfluidic-based circulation-on-a-chip model that reproduces key physiological hydrodynamic features of blood vessels to investigate how disseminated cancer cells survive under this mechanical stress. To optimize our system and demonstrate that we are accurately modeling physiological shear stress, we performed experiments by varying the flow rate, diameter, and viscosity. Using this system, we examined the survival of several cancer cell lines derived from five different solid tumors, including those from both primary and metastatic tumors. Our results demonstrate that aggressive cell lines survive significantly more than non-aggressive ones in all solid tumors included in this study. However, we also show that this survival does not always correlate with the site of origin (primary or metastatic cell lines). Consequently, these results provide proof of principle for a novel circulation-on-a-chip model, which offers a suitable tool for studying the metastatic potential of CTCs in a reliable and ethically preferable manner. Not only that, but it also provides a platform for further investigating the mechanisms underlying the enhanced survival of CTCs and the effects of mechanical stress during metastasis, thereby avoiding the use of *in vivo* models.

POSTER 68 presented by:

NAME: Aina Albajar Sigalés

Studying the mechanical regulation of nucleocytoplasmic transport using Single Molecule Tracking

Aina Albajar-Sigalés [1,2], Anabel-Lise Le Roux [1], Valeria Venturini [1], Roger Pons [3], María F. García Parajo [3,4], Sílvia Pujals [5], Amy E.M. Beedle [1,6], Pere Roca-Cusachs [1,2]
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Cellular function relies on the precise regulation of macromolecular transport between the cytoplasm and the nucleus, a process governed by Nuclear Pore Complexes (NPCs). While traditional understanding held that transport through NPCs was mainly dictated by the physicochemical properties of the transported molecules, recent research has revealed an additional layer of regulation driven by mechanical forces. Whether applied directly or transmitted through the cytoskeleton, mechanical signals have the capacity to deform the nucleus and, consequently, alter the conformation of NPCs, increasing their diameter. This changes nucleocytoplasmic transport rates and impacts the localisation of a variety of signalling molecules. However, the cellular components responsible for force transmission to NPCs as well as the spatial distribution of this effect throughout the nuclear envelope, remain poorly understood. Here, we aim to answer these questions by investigating whether isolated nuclei, a minimal system depleted of all the cell's cytoplasmic machinery, still exhibit mechanosensitive nucleocytoplasmic transport. To do so, we apply mechanical force by confining isolated nuclei to a certain micrometre height and, simultaneously, measure nucleocytoplasmic transport rates by tracking individual dextran molecules translocating through NPCs. Our results show that molecules translocate faster in confined nuclei, suggesting that unspecific force application to a passive nuclear envelope is enough to induce conformational changes in NPCs and alter transport dynamics.

POSTER MECHANOBIOLOGY

POSTER 69 presented by:

NAME: Mariana Azevedo Gonzalez Oliva

Piezo1 regulates the mechanotransduction of soft matrix viscoelasticity

Azevedo Gonzalez Oliva, Mariana [1,2]; Ciccone, Giuseppe [1,2]; Flaschner, Gotthold [1]; Vassalli, Massimo 2; Roca-Cusachs, Pere [1]; Salmeron-Sanchez, Manuel [1,2]
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Mechanosensitive ion channels, such as Piezo1, have emerged as having fundamental roles in sensing the mechanical properties of the extracellular matrix (ECM). However, whether and how Piezo1 senses viscoelasticity—the time-dependent mechanical behavior characteristic of soft tissues like the brain—remains unclear. To address this question, we combined an immortalised mesenchymal stem cell (MSC) line in which Piezo1 expression can be modulated with soft and stiff viscoelastic hydrogels that have independently tuneable elastic and viscous moduli. We demonstrate that Piezo1 is a mechanosensor of viscoelasticity in soft ECMs, both experimentally and throughout simulations using a modified viscoelastic molecular clutch model that incorporates Piezo1. Using RNA sequencing, we also identify the transcriptomic phenotype of MSC response to matrix viscoelasticity and Piezo1 activity, identifying gene signatures that modulate MSC's mechanobiology in soft and stiff viscoelastic hydrogels. These findings advance our understanding of how cells interpret time-dependent mechanical cues and position Piezo1 as a central transducer of viscoelasticity in soft tissues. Given the highly viscoelastic nature of brain tissue, our work provides a potential mechanistic framework for Piezo1's involvement in neural tissue physiology and pathophysiology, and offers new avenues for engineering brain-like *in vitro* models to probe neural mechanobiology and disease.

POSTER 70 presented by:

NAME: Pol Picón Pagès

Mechanistic Insights into GPR133 Signaling in Glioblastoma Multiforme

Picón-Pagès, Pol [1,2,3,4], Brkiç, Tamara [1,2,3,4], de Cecco, Elena [5], Aguzzi, Adriano [5], del Río, José Antonio [1,2,3,4]
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Glioblastoma multiforme (GBM), a World Health Organization grade IV astrocytoma, is among the most aggressive and prevalent primary brain malignancies, with a dismal five-year survival rate of approximately 7%. Despite general improvements in brain tumor survival over recent decades, GBM outcomes remain poor due to the tumor's intrinsic heterogeneity and the limited efficacy of current standard-of-care treatments. One of the distinguishing molecular hallmarks of GBM is the aberrant de novo expression of the adhesion G protein-coupled receptor (aGPCR) GPR133, particularly in the hypoxic core of the tumor. Notably, GPR133 expression has been shown to be essential for GBM cell survival. In our laboratory, we have developed novel U87MG CRISPR-engineered cell lines with enhanced expression of native aGPCRs via promoter modulation. Upon comparing GPR56, GPR126, and GPR133 overexpression models with the parental U87MG line, we observed a distinct morphological phenotype exclusive to the GPR133 CRISPR-modified cells. These cells exhibited enhanced mechanotransduction, beginning with increased cell adhesion mediated by focal adhesion kinase (FAK) phosphorylation, altered tubulin expression levels, and a shift in Yes-associated protein (YAP). In conclusion, we present the first known model of native GPR133 overexpression in GBM cells. By elucidating its molecular mechanisms, we aim to better understand GBM behavior and contribute to the development of novel therapeutic strategies targeting this lethal disease.

POSTER MECHANOBIOLOGY

POSTER 71 presented by:

NAME: Ona Baguer Colomer

Role of nuclear mechanics in the regulation of EMT in pancreatic cancer cells

Ona Baguer [1,2], Laura M. Faure [1], Mikhail Chesnokov [3], Gotthold Fläschner [1], Sladjana Zagorac [3], Francisco X. Real [3,4], Pere Roca-Cusachs [1,2]

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Pancreatic cancer is associated with a strong desmoplastic reaction, leading to a stiffening of the tissue that is known to induce the onset of the epithelial-to-mesenchymal transition (EMT). Both tissue stiffening and EMT are strongly associated with changes in cell and nuclear shape. In turn, nuclear shape changes (i.e., nuclear deformations) are known to trigger nuclear mechanotransduction. This suggests that tissue stiffening, EMT, and nuclear mechanotransduction could be related, but if and how this relationship occurs is unknown. By combining hydrogels of varying rigidities, genetic tools to alter the nuclear mechanical properties, and a chemical EMT inducer (TGF-β1), our preliminary data indicate that nuclear mechanics modulates pancreatic cancer cell responses to both substrate stiffness and TGF-β1, potentially revealing a nuclear mechanotransduction mechanism involved in EMT regulation.

POSTER 72 presented by:

NAME: Carolina Rodríguez-Gallo

Magnetic actuators: Inducing stretching in functional 3D muscle human engineered models

Carolina Rodríguez-Gallo, Xiomara Fernandez-Garibay, Juanma Fernandez Costa, Javier Ramon Azcon
IBEC

3D tissue bioengineering has recently risen as a new paradigm offering more complex biological models. Opening the door to modifying the cell environment has already demonstrated the recovery of tissue morphology, cell differentiation, and functionality[1]. The most used 3D model of human skeletal muscle tissues is based on human myoblasts encapsulated in a biomaterial compacted around two flexible biocompatible pillars. The matrix's contraction promotes cell alignment along the line connecting the two pillars, producing long multinucleated myofibers. This 3D architecture allows for measuring muscle-generated force by assessing the displacement of the flexible pillars after electrical stimulation of the muscle. This system has demonstrated the ability to replicate protein expression profiles involved in myogenic differentiation and sarcomere function, model pathophysiological processes in neuromuscular diseases [2], and identify potential therapeutic targets.

Despite its significant advantages, the system presents many potential functionalities that have not been explored. For instance, the environmental stiffness is fixed, and the tissues can only be electrically stimulated. This project aims to overcome these limitations through the following research objective.

We aim to create a new platform that allows for modifying environmental stiffness and the induction of both stretching and contraction in the tissue. The effects of these two mechanical actuations on muscle tissue have not yet been explored in the literature. The proposed solution is based on embedding magnetic particles within the flexible pillars supporting the tissue. By aligning the magnetic moment of these particles, we can induce the bending of the pillars in response to an external magnetic field [3]. In addition, by varying the strength of the magnetic field, we can fine-tune the force applied to the tissue. This innovation will open avenues for numerous research projects, including systematically investigating the tension-differentiation relationship and inducing fiber damage. Additionally, it will facilitate the discovery of new disease phenotypes and outcomes, which can be leveraged for subsequent drug screening assays.

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POSTER 73 presented by:

NAME: Miguel González Martín

Designing mechanosensible molecules for the mechanical control of cellular transcription

Miguel González-Martín [1,2,3], Juan Martin Portilla [2,4], Ignasi Granero-Moya [1,2,3], Dimitrije Ivančić [2,4], Marc Molina Jordán [1,2,3] , Ion Andreu [5,6], Marc Güell [2,4], Pere Roca-Cusachs [1,2,3].

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Cells interpret mechanical cues from their microenvironment through mechanotransduction, activating signaling pathways that regulate diverse aspects of cellular behavior. However, engineering these pathways in a controllable and predictable manner remains a major challenge. Here, we present a strategy to develop a synthetic mechanosensitive transcription factor (mSynTF) that links mechanical inputs to targeted gene expression. This system exploits the force-induced changes in nucleocytoplasmic transport, enabling mechanical perturbations at the nuclear envelope to drive transcriptional responses. By tuning both passive and facilitated transport properties of the mSynTF, we aim to recapitulate the localization dynamics of endogenous mechanosensitive regulators such as YAP and Twist, while conferring precise transcriptional control over synthetic gene targets. To identify effective mSynTF variants, we established a high-throughput screening platform using substrates with defined stiffness profiles, allowing us to isolate candidates with robust mechanosensitive behavior. Downstream characterization of these candidates will elucidate the structural and functional determinants of transcription factor mechanosensitivity. Overall, this work establishes a modular framework for mechanical regulation of gene expression, providing a foundation for a state-of-the-art directed evolution platform and enabling the integration of mechanotransduction into synthetic gene circuits. This approach opens new avenues for employing mechanical signals in advanced synthetic biology applications, offering a minimal yet powerful toolset for programmable, force-responsive gene control.

POSTER 74 presented by:

NAME: Montserrat Sales Mateo

Electrochemical Tunneling Spectroscopy Study of Charge Transport in the Redox Protein Plastocyanin, its pH Dependence, and Copper Ion Role

Gustavo A. Echeveste Salazar [1,2], Montserrat Sales-Mateo [1,2,3], Núria Camarero [1,2], Marina I. Giannotti [1,2,4], Pau Gorostiza [1,2,5]

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Plastocyanin (Pc) is a copper-containing redox protein involved in the photosynthetic electron transfer (ET) chain, transferring electrons from cytochrome to Photosystem I. Previous electron transport (ETp) studies using Electrochemical Scanning Tunneling Microscopy (ECSTM) have shown that the current between Pc and its partner (photosystem I) displays a distance decay of several nanometers through the aqueous solution, spanning beyond the tunneling regime [1]. These results suggest a more complex mechanism than direct quantum tunneling of electrons between the redox active sites.

One possibility is that solution ions (including protons) are involved in the ETp process by assisting the charge transport process [2]. This idea can be tested by measuring the behavior of Pc at different pH values. To achieve this, we attached a terminal cysteine mutant of Pc (ensuring precise orientation) to an atomically flat Au (111) electrode, and used ECSTM to record current-distance curves (I-z) at different pH values and in the absence or the presence of the copper ion in Pc. In each condition, we used the distance decay rate of the current (β, nm-1) to quantify the ETp behavior of Pc for the first time by ECSTM spectroscopy.

Statistical analysis of the results yields lower β values (longer-extending currents) at higher pH both with apo-Pc (plastocyanin protein without Cu) and holo-Pc (plastocyanin protein with Cu). A similar trend with pH is also observed in experiments in Au (111) alone, but the β values here are higher (β > 7 nm-1, in a range compatible with electron tunnelling between the ECSTM probe and Au (111) sample) than in Pc. These results support the observations reported in [1] for Pc-PSI and reveal the pH dependence of Pc ETp.

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POSTER MECHANOBIOLOGY

POSTER 75 presented by:

NAME: Steffen Grosser

Mechanical polarity in cell migration

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Cells migrate on elastic substrates in the absence of any net force, which poses a fundamental challenge in the field of cell dynamics. All forces transmitted from the cells to the substrate cancel out, and neither force magnitude nor force dipole are related to neither cell speed nor direction. In two recent studies on epithelial cell motility [1,2], however, we have found that a higher moment of the cell traction distribution, the quadrupole, is in fact closely related to cell velocity (both speed and direction). The quadrupole characterizes the asymmetry of the traction distribution, even when the total net force cancels out. Experimentally, this quadrupole-velocity relation holds 1) for single cells and for short multicellular trains, 2) for MDCK as well as for MCF-10A cells, 3) for optogenetically activated cells just as for spontaneously motile cells, and 4) even for cells moving along gradients of adhesion.

To interpret this traction asymmetry, we propose to decompose the force patterns into an active, unbalanced part that drives cell motion, and a frictional component. Using an active gel model, we show how this leads to a novel, actual force-velocity relation for cell dynamics.

POSTER 76 presented by:

NAME: Jordi Comelles

Long-range organization of primary intestinal fibroblasts guides directed and persistent migration of organoid-derived intestinal epithelia

Jordi Comelles [1,2,9], Aina Abad-Lázaro [1,9], Verónica Acevedo [1], David Bartolomé-Català [1], Aitor Otero-Tarrazón [1], Anna Esteve-Codina [3,4], Xavier Hernando-Momblona [5,6], Eduard Batlle [5,6,7], Vanesa Fernández-Majada [1], Elena Martinez [1,2,8,10*]*

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** Correspondence*

Fibroblasts reside underneath most epithelial tissues. In the intestine, recent studies have shown that fibroblast migration contributes to vilification and wound healing. Yet, whether physical interactions between epithelial cells and fibroblasts contribute to epithelial movement remains elusive. Here, we show that intestinal fibroblasts enhance directed and persistent migration of organoid-derived intestinal epithelia. Using a gap closure *in vitro* model of the intestinal mucosa, we demonstrate that direct contact with fibroblasts improves gap closure by promoting cell alignment, sustaining tissue integrity, and synchronizing crypt–villus migration. Fibroblasts undergo long-range ordering to align perpendicularly to the epithelial front and deposit protein paths that act as guidance features to direct epithelial migration. In parallel, epithelial cells acquire a wound-associated epithelial-like phenotype, but insufficient to explain the effects of fibroblast contact. Our findings uncover a dual role for intestinal fibroblasts in epithelial repair, coordinating both biochemical and physical cues to ensure efficient and cohesive migration.

POSTER MECHANOBIOLOGY

POSTER 77 presented by:

NAME: Amélie Godeau

Two phases of invasion associated to trophoblast differentiation in autonomous human embryo implantation

Amélie Luise Godeau [1], Laura Parra [1], Julia Faba Costa [1], Ot Massafret [1], Marc Casals [1], Ester Aroca [1], Albert Parra [1], Anna Ferrer-Vaquer [1], Miquel Solé [2], Montse Boada [2], Anna Seriola [1], Samuel Ojosnegros [1]

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During implantation, the human embryo attaches to the endometrial lining of the maternal uterus with the polar trophectoderm. Trophoblast cells at the site of attachment initiate invasion into the underlying endometrial stroma, differentiating into cytotrophoblasts and syncytiotrophoblasts. These specialized cells establish connections with the maternal tissue and vasculature, ultimately contributing to the formation of the placenta. In this study, we introduce a novel ex vivo approach combining hydrogel-based culture and traction force microscopy to quantify the mechanical forces exerted by human embryos during implantation. Human embryos exhibit characteristic interstitial implantation behavior, embedding deeply within the extracellular matrix and actively remodeling it while generating traction forces. Implantation proceeds in two distinct phases: an initial rapid penetration phase, characterized by increased growth rate and lower total force and displacement, followed by a slower invasive phase with higher cumulative traction forces. In-plane displacements consistently converge radially toward the embryo center, while out-of-plane displacements are initially negative and progressively shift to upward (positive) values during the course of invasion. At later stages, regions exhibiting positive out-of-plane displacement display dynamic fluctuations, with localized reversals in displacement direction—reflecting spatially heterogeneous and temporally dynamic force remodeling of the matrix. These change of mechanical pattern correlates with spatial segregation and differentiation of trophoblast subpopulations: formation of large, hCG-positive syncytiotrophoblasts and smaller, stress fiber–rich pre-extravillous trophoblast (pre-EVT) cells. Together, these results suggests that human embryo implantation follows a coordinated spatiotemporal invasion program coupled to lineage-specific trophoblast differentiation.

POSTER 78 presented by:

NAME: Clément Hallopeau

Mechanical confinement controls stemness and cell flows in the intestinal crypt

Hallopeau, Clément [1], Ceada, Gerardo [1], Taelman, Jasin [3], Diaz Ferrer, Monica [3], Menendez, Anghara [1], Palomo, Sergio [2], Gomez Gonzalez Manuel [1], Moraitis, Ilias [3], Batlle, Eduard [2], Guiu Jordi [3], Pérez Gonzalez, Carlos [3], Trepat, Xavier [1]
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The intestinal epithelium is a highly dynamic tissue that maintains a tight compartmentalization of cell types despite continuous cell flows across compartments. This compartmentalisation integrates different biochemical cues along the crypt-villus axis. Regionalized Wnt and BMP signaling set the compartments size while opposed gradients of Eph and ephrin set the compartments boundary. Here we show that self-organized mechanical confinement also plays a critical role in regulating intestinal cell stemness. We show that knocking out EphB2 and EphB3 disrupts mechanical confinement, decreasing pressure at the stem cell niche and friction at the crypt boundary. In parallel, the stem cell niche expands against the enterocyte domain, mainly through an increase in proliferation. We show, further, that the loss of mechanical confinement entails aberrant differentiation, characterized by a drop in stemness and the emergence of long-lived transitional states. Our data supports that this abnormal differentiation arises from both scattering of Paneth cells and direct mechanotransduction. Together, these findings identify mechanical confinement as a key regulator of stemness in the intestinal epithelium.

FLASH PRESENTATION | NANOMEDICINE

FLASH 79 presented by:

NAME: Kristin Fichna

Nanomotor-Assisted intravesical chemotherapy for bladder tumor reduction and recurrence prevention

Fichna, Kristin [1,2], Crespo-Cuadrado, Maria [1], Konuparamban, Acsah [3], Di Carlo, Valerio [1], Esporrín-Ubieto, David [1], Macías Tarrío, Ines [1], Chen, Shuqin [1], Gómez-Martínez, Maria [3], Bakenecker, Anna [1], Vilaseca, Antoni [4], Llop, Jordi 3, Sánchez Ordóñez, Samuel [1,5]

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Bladder cancer is among the most prevalent cancers worldwide. Intravesical administered chemotherapeutic agents are the current adjuvant standard of care after surgical resection of the bladder tumor. However, their efficacy is limited by poor retention in the bladder and inadequate fluid mixing capabilities leading to poor oncological results and high relapse rates. This highlights the urgent need for innovative drug carriers to enhance the therapeutic efficiency of these chemotherapeutic agents. Here, we present urease-powered nanomotors based on mesoporous silica nanoparticles loaded with Mitomycin C (MMC), the gold standard in bladder cancer chemotherapy. These nanomotors exhibit self-propulsion in the presence of bioavailable concentrations of urea, enabling active drug delivery to the bladder tumor. Remarkably, the loading of MMC does not impair the nanomotors' motion capabilities. *In vitro*, spectral flow cytometry analysis showed that active nanomotors at biocompatible concentrations internalize 2.3 times more efficiently into mouse bladder cancer cells than non-motile nanoparticles. Toxicity studies further revealed that these active drug-loaded nanomotors reduce cancer cell viability 19.25-times more efficiently than the free drug. *In vivo* results highlight that, unlike free Mitomycin C, urease-powered nanomotors loaded with the drug not only significantly reduce bladder tumor volumes but also prevent tumor recurrence, demonstrating their potential to tackle major challenges in bladder cancer chemotherapy.

FLASH 80 presented by:

NAME: Marco Basile

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

Marco Basile [1,2,3], Cátia Lopes [1,2], Matilde Ghibaudi [1], Nicola Manicardi [1,4], Lorena Ruiz Perez [1,2,5], and Giuseppe Battaglia [1,2,3,5,6]

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

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

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

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

FLASH PRESENTATION | NANOMEDICINE

FLASH 81 presented by:

NAME: Tomás Quiroga

Deep indel mutagenesis of the ALS protein SOD1 to comprehensively map the impact of mutations on protein abundance and dimer formation

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Mutations in SOD1 cause Amyotrophic Lateral Sclerosis (ALS) through diverse mechanisms, including destabilization, dimer-dissociation, aggregation, and neurotoxicity, but the functional consequences of most variants remain uncharacterized. To systematically assess the impact of all possible amino acid mutations in SOD1, we performed deep mutational scanning to measure their effect of 6000 variantss on protein stability (abundance) and dimerization (binding). The two phenotypes show a strong global correlation (R ~ 0.90), indicating that destabilizing mutations also impair binding. However, we identify a subset of outlier variants that deviate from this trend, many of which localize at the dimer interface, suggesting they specifically alter binding without broadly affecting stability. We observe that substitutions in buried β-strands are highly destabilizing, whereas loops, especially longer ones involved in metal binding, show greater mutational tolerance. Insertions and deletions are globally disruptive. Zn-binding residues are particularly sensitive, underscoring their functional relevance. Our dataset includes quantitative scores for all known SOD1 pathogenic and uncertain significance variants (VUS). We find that 82% of pathogenic variants and 75% of VUS reduce protein stability, while 71% of unreported variants are also destabilizing. Importantly, the addition of binding data uncovers variants that are stable yet defective in dimerization, highlighting alternative mechanisms of dysfunction. Overall, our results provide a comprehensive atlas of SOD1 mutational effects and suggest that both stability and binding contribute to pathogenicity, offering a potential resource for variant classification in ALS.

FLASH 82 presented by:

NAME: Tiziana Russo

A LEGO® like approach to i-combisomes origami

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Vesicles are nano- to micro-scale self-enclosed structures assembled from amphiphiles that form lamellar lyotropic phases. They are ubiquitous in nature and play a fundamental role in numerous biological processes such as endocytosis, exocytosis, and intercellular communication. While the influence of vesicle chemical and physical properties has been extensively studied, the impact of their morphology remains underexplored. Vesicles can adopt a wide range of shapes driven by bilayer asymmetries, incorporation of non-zero curvature components, and variations in the reduced volume-to-area ratio. However, generating faceted or non-spherical vesicle morphologies has required complex synthetic strategies, hindering the generation of vast libraries of amphiphiles.

Here, we introduce a modular and versatile strategy for inducing morphological polymorphism in vesicles using a new class of supramolecular amphiphiles—ionically-linked comb polymers (iCPs). These amphiphiles consist of a hydrophilic polymer backbone to which hydrophobic ligands are non-covalently complexed via simple acid-base interactions. This design enables facile exchange of ligands, allowing for the generation of vesicles with diverse morphologies—termed i-combisomes—analogous to building with LEGO® bricks. We utilized a (poly(CBAA-co-DMAPAA)) backbone to which we complexed six different ligands: mono-dodecyl hydrogen phosphate, di-dodecyl hydrogen phosphate, di-tetradecyl phosphate, di-hexadecyl phosphate, dodecyl benzene sulfate and 3,4,5-tris(dodecyloxy)benzene sulfonic acid. With a combination of confocal laser scanning microscopy (CLSM), cryogenic transmission electron microscopy (Cryo-TEM) and molecular dynamics (MD) simulations we correlated iCPs molecular design to the membrane properties, deriving designing rules to achieve polymorphism. We further prove i-combisomes versatility by testing their ability to fuse with their biological counterpart: DLPC GUVs and extra-cellular vesicles (EVs). These findings lay the foundation for the development of synthetic cells with different properties and morphologies, paving the way for the design of synthetic vesicles with programmable properties.

FLASH PRESENTATION | NANOMEDICINE

FLASH 83 presented by:

NAME: Claudia Camarero

Disrupting protein aggregation as a novel strategy against malaria: mechanistic insights into YAT2150

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The malaria parasite's ability to develop drug resistance is rapidly undermining existing treatments, highlighting an urgent need for novel antimalarials. A promising strategy involves targeting protein aggregation, a fundamental and essential process throughout the parasite's life cycle. Disrupting this process significantly weakens *Plasmodium falciparum*, the parasite responsible for the most severe form of malaria, pointing to its critical yet underexplored role in parasite's biology. A groundbreaking compound, YAT2150, a bis(styrylpyridinium) salt, shows great promise as a novel antimalarial agent, as it exhibits potent antiplasmodial activity in the low nanomolar range, even against drug-resistant strains, by interfering with protein aggregation in the parasite. To gain a comprehensive understanding of this compound's mode of action and uncover critical elements involved in parasite survival, a multi-omics strategy is being employed. Since *in vitro* resistance to YAT2150 has not yet been observed, highlighting the compound's robustness but making this strategy not informative for target identification, a combination of complementary techniques is being employed. This multi-approach includes pull-down assays with biotinylated derivatives, proteomic approaches such as Cellular Thermal Shift Assays (CETSA), and transcriptomic analyses. Together, these methods aim to identify YAT2150's direct molecular targets and elucidate its downstream biological effects. Preliminary findings demonstrate widespread target dysregulation, consistent with the compound's overall mechanism of action, with motility related based mechanisms, such as microtubule-based processes and actin filament organisation being some of the significantly affected biological functions. The final stage will involve validating these targets through genetic manipulation of *P. falciparum*. By integrating biochemical, genetic, and cell biological approaches, this comprehensive research will not only clarify YAT2150's mechanism of action but also enhance our understanding of protein aggregation in Plasmodium's biology, potentially paving the way for novel malaria therapies.

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FLASH 84 presented by:

NAME: Carles Prado Morales

Breaching the human skin barrier with degradable enzymatic nanobots

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

Nanobots (NBs), self-propelled nanoparticles, have recently emerged as next-generation advanced carriers. These types of NBs have demonstrated enhanced drug delivery capabilities in two-dimensional cell cultures, increased cellular uptake, improved diffusion in viscous media, effective penetration of mucosal barriers, and tumor infiltration *in vitro*. Moreover, *in vivo* studies have shown that they can accumulate at bladder tumor sites, resulting in up to a 90% reduction in tumor size.

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

POSTER NANOMEDICINE

POSTER 85 presented by:

NAME: Jordi Alcalà Barrat

Effect of UV Irradiation and Humidity on the Electrical Conductivity of Cable Bacteria Sheaths

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Cable bacteria are multicellular microorganisms capable of long-distance electron transport via highly conductive fibers embedded in their cell envelope [1,2]. While their conduction mechanism has been extensively studied under physiological and ambient conditions [1,3], the effect of environmental stressors on their electrical performance remains underexplored. Here, we investigate by means of microelectrode current-voltage measurements the electrical conductivity of isolated cable bacteria filaments under varying atmospheric conditions: humid ambient air, nitrogen atmosphere, and combinations of them with ultraviolet (UV) irradiation.

Consistent with previous findings, conductivity gradually degrades under ambient humid conditions, remains stable or recovers slowly in dry N_2 [4] and is very stable in vacuum conditions [2]. Furthermore, we find that UV irradiation significantly accelerates the degradation of conductivity under ambient humid conditions, whereas no substantial effect is observed under dry ambient conditions. These findings suggest a synergistic effect between oxygen and UV-induced damage to the conductive structures, likely related to oxidative degradation. Our results provide new insight into the environmental robustness of the cable bacteria conduction system and highlight the importance of controlling both chemical and photonic factors in bioelectronic applications.

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POSTER 86 presented by:

NAME: David Esporrín Ubieto

Enzymatic nanomotors based on chemically-crosslinked nanogels with enhanced motion in viscous media for biomedical applications

David Esporrín-Ubieto [1], Noelia Ruiz-González [1], Valerio Di Carlo [1], Daniel Sánchez-deAlcázar [1], Florencia Lezcano [1], Anna Pushkareva [1], Samuel Sánchez [1,2,]*

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Targeted drug delivery remains a central challenge in biomedical research, particularly due to the difficulty of navigating through highly viscous biological fluids such as mucus and synovial fluid. A promising solution has emerged in the form of self-propelled nanoparticles, or nanomotors (NMs), which can actively move through such environments. Among these, silica-based NMs have been widely studied, thanks to their well-established synthesis. However, their high density and limited water solubility pose challenges in biological contexts. This talk explores the transition from inorganic NMs to next-generation organic-based systems. In particular, we highlight the potential of responsive nanogels, chemically cross-linked polymer networks, as biocompatible NMs. They can alter their size and hydrophilicity in response to environmental cues such as pH, temperature, and redox conditions, significantly enhancing their mobility through viscous media. Their tunable properties not only improve propulsion but also reduce undesirable interactions with surrounding tissues. Finally, we will showcase their applications, from synthesis and *in vitro* testing to *in vivo* imaging using advanced.

POSTER NANOMEDICINE

POSTER 87 presented by:

NAME: Valentino Barbieri

Harnessing Structural Complexity for Phenotypic Targeting

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Since the introduction of the concept of superselectivity [1], targeting strategies based on weak multivalent ligand–receptor interactions have emerged as powerful alternatives to conventional drug design. Unlike high-affinity targeting, which often results in nonspecific uptake due to indiscriminate receptor binding, multivalency enables selective engagement only under specific biological conditions, offering superior selectivity and specificity. Our phenotypic targeting strategy capitalizes on this principle by leveraging characteristic cellular features, such as receptor expression and membrane structure, to guide nanoparticles toward diseased tissues with high selectivity.

This approach proves particularly beneficial in pathologies affecting tissues protected by physiological barriers, where traditional ligand-based targeting often falls short. Notably, we previously demonstrated the effectiveness of our strategy for BBB crossing [2] [3] in the context of amyloid beta clearance.

By shifting the focus from isolated receptors to the broader biological context, phenotypic targeting requires sophisticated nanoparticle engineering [4]. We achieve this through supramolecular self-assembly of amphiphilic block copolymers, enabling the creation of peptide-functionalized polymeric nanoparticles with tunable avidities, immune evasion capabilities, and fine-tuned biological interactions.

In our design, the hydrophilic corona plays a multifunctional role; beyond imparting stealth, it modulates ligand accessibility and mediates repulsive interactions with the glycocalyx, enhancing selective engagement. Furthermore, the modularity of our supramolecular platform enables us to generate asymmetric morphologies and control the spatial distribution of ligands, thereby better reflecting the heterogeneous presentation of receptors on cell surfaces.

These design elements are coupled with integrated barcoding strategies, enabling unique identification of nanoparticle formulations and facilitating high-throughput assessment of their targeting performance in vitro and in vivo. Our experimental data can then be fed into our theoretical framework to inform the rational development of next-generation nanomedicines. Ultimately, our work aims to establish design principles that enable precise, context-driven, and personalized therapeutic delivery through phenotypic targeting.

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POSTER 88 presented by:

NAME: Inés Macías Tarrío

Biocompatible nanobots for personalized bladder cancer therapy: mechanisms of action and therapeutic efficacy

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

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The effective delivery of anticancer drugs is challenged by drug degradation, poor tumor penetration, and limited targeting. Enzyme-powered nanobots (NBs) or self-propelled nanoparticles, have emerged as promising tools to address these issues. Specifically, Urease powered NBs are capable of move towards the bladder using the available urea, which makes them ideal for treating bladder cancer (BC), a disease with high recurrence and poor long-term survival. These NBs improve tumor retention and drug delivery compared to passive systems. However, most current designs rely on inorganic materials and conventional drugs, highlighting the need for more biocompatible and personalized NB platforms. Herein, we present urease-powered nanobots (NBs) based on poly(lactic-co-glycolic acid) (PLGA), an FDA- and EMA-approved biodegradable polymer, designed for targeted bladder cancer (BC) therapy. These NBs were loaded with a selective inhibitor of fibroblast growth factor receptor 3 (FGFR3), a protein commonly overexpressed in BC patients, and functionalized with urease to enable autonomous motion in the presence of urea. We evaluated the biocompatibility, fuel-responsive motility, and cellular uptake of the NBs. Following treatment, we assessed cell viability, apoptosis induction, and alterations in cell cycle progression. To explore translational potential, we conducted *in vivo* experiments in tumor-bearing mice, administering the drug-loaded NBs intravesically and monitoring tumor volume and survival for two months. Our results demonstrate that NBs are biocompatible, exhibit high drug-loading efficiency, and become self-propelled in urea-rich environments. Compared to passive particles, the urease-powered NBs achieved significantly enhanced cellular uptake. Furthermore, drug-loaded NBs induced rapid apoptosis, reduced the drug's IC50 by eight-fold, and caused cell cycle arrest on S-phase. *In vivo*, treated mice exhibited tumor regression, resulting in survival improvement compared to untreated mice. Collectively, these findings demonstrate the potential of our NBs as a highly effective, biocompatible and personalized platform for bladder cancer intravesical therapy.

POSTER NANOMEDICINE

POSTER 89 presented by:

NAME: Giulia Porro

Studying LRP1 endocytosis and recycling kinetics at the BBB in Alzheimer's disease

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The blood-brain barrier (BBB) is a highly selective barrier composed by specialised brain endothelial cells (BECs) lining the brain vasculature. The BBB prevents the entry of toxins and pathogens into the brain while tightly regulating the transport and signalling of macromolecules. Among its key regulators is the low-density lipoprotein receptor-related protein 1 (LRP1), mainly expressed by BECs, an essential transporter mediating the transcytosis of various ligands, including amyloid-ß (Aβ) peptide, whose accumulation is a hallmark of Alzheimer's disease (AD). Reduced LRP1 expression and altered endocytic trafficking have been implicated in impaired Aβ clearance and subsequent neurodegeneration. However, the kinetics of LRP1 endocytosis and recycling at the BBB remain poorly defined, particularly under inflammatory conditions that mimic AD pathology. This project investigates the kinetics underlying the dynamic regulation of LRP1 surface expression and its intracellular trafficking under both physiological and inflammatory conditions. *In vitro*, LRP1 internalisation and recycling are quantified in BECs through surface biotinylation-based assays coupled with ELISA detection. To simulate the inflammatory stress associated with AD, BECs are treated with Aβ monomers, oligomers, and fibrils to assess their effects on LRP1 trafficking kinetics and dynamics and its surface expression. Preliminary data suggest rapid endocytosis within the first 10 minutes, followed by a reduced but detectable rate of internalisation at longer time points. In parallel, microscopy-based techniques, such as proximity ligation assay (PLA), are applied to ex vivo tissue sections from age-matched wild-type and 3xTg-AD transgenic mice at different disease stages. The technique evaluates the spatial co-localisation of LRP1 with Rab GTPases markers - Rab5, Rab7, and Rab11 - which define early, late, and recycling endosomes, respectively, in the context of AD progression. Overall, this study will provide a strong basis for future development of targeted strategies to modulate these molecular processes and explore new therapeutic approaches for neurodegenerative disorders.

POSTER 90 presented by:

NAME: Ainhoa González Caelles

Engineered PLGA Nanobots for RNAi-Based Treatment of Bladder Cancer

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Gene therapy has emerged as a highly promising strategy for targeted cancer treatment by selectively silencing genes involved in tumor development and progression, particularly with small interfering RNA (siRNA). Despite its potential, the clinical translation of siRNA-based therapeutics remains limited by challenges, such as effective delivery due to the susceptibility to enzymatic degradation and poor cellular uptake. To overcome these barriers, the development of advanced delivery systems capable of protecting the siRNA cargo and ensuring its delivery to the cells with high efficiency is essential. Nanoparticles (NPs) have gained relevance as delivery tools for siRNA due to their customizable properties, biocompatibility, and ability to encapsulate nucleic acids. Nanobots (NBs), NPs functionalized with an enzyme on the surface that provides them self-propulsion and enhanced fluid mixing capabilities, can significantly improve drug delivery and therapeutic outcomes. In our approach, the employed enzyme is urease, that uses urea as a bioavailable substrate, making these NBs an ideal platform for bladder cancer therapy. Notably, recent studies have demonstrated significant tumor accumulation of urease-powered NBs in a bladder cancer mouse model, and their ability to deliver efficiently pDNA, supporting their potential as a therapeutic agent. Bladder cancer (BC) remains a serious global health concern, with high incidence and mortality rates. Most cases are non-muscle-invasive bladder cancer (NMIBC), a type known for its high recurrence and limited response to current treatments. Standard therapies, such as intravesical drug administration, chemotherapy, surgery, and Bacillus Calmette-Guérin (BCG) immunotherapy, often lead to poor efficacy and notable side effects, highlighting the urgent need for novel therapeutic approaches. In this context, Nanobot-based therapies present a promising alternative. This study focuses on the development and *in vitro* characterization of urease-powered NBs for the delivery of siRNA to bladder cancer cells. The NBs were synthesized using biocompatible and biodegradable poly(lactic-co-glycolic acid) (PLGA) nanoparticles as scaffold. A layer-by-layer (LbL) assembly strategy was used to load selected siRNAs onto the PLGA surface, targeting genes involved in bladder cancer progression and immune modulation. Urease was subsequently incorporated to confer self-propulsion, completing the full NB design. The performance of the urease-powered NBs was evaluated through a series of *in vitro* experiments, including assessments of their motion behavior, siRNA delivery efficiency, gene silencing capability, and cytotoxicity. The results confirmed the successful synthesis of NBs with favorable physicochemical properties, efficient motion in urea-rich environments, and effective siRNA delivery. In conclusion, urease-powered NBs represent a highly promising platform for siRNA delivery in bladder cancer treatment. By using urea as a substrate, abundantly present in the urinary tract, these NBs offer a biocompatible and efficient alternative to conventional therapies. This study advances the field of nanomedicine and highlights the potential of NBs as a versatile and effective approach for the treatment of bladder cancer and other malignancies.

POSTER NANOMEDICINE

POSTER 91 presented by:

NAME: Dario Castellana

Radioprotection and Tissue Regeneration in resectable Head and Neck Squamous Cell Carcinoma

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In Head and Neck squamous cell carcinoma cases, buccal mucosa regeneration after ablative surgery and radioprotection against X-ray treatment can improve both treatment's efficacy and its outcome during clinical therapy. We aim to develop an injectable hydrogel and a biodegradable electrospun fibers mat to trigger a local co-administration of two therapeutic compounds: (i) an FDA approved radio-protective drug and (ii) tissue-stimulating ions. Amifostine is the selected pro-drug and it will be encapsulated in PLGA modified nanoparticles (NPs) further embedded in the hydrogel, while the therapeutic ions-based nanoparticles will be loaded in PLA fibers and delivered over a time span of 30 Days. Amifostine has been encapsulated within PLGA, the viability of human dermal fibroblast upon administration of amifostine-enriched NPs is as high as 90% or above. The drug's encapsulation efficacy reached around 80% and it will enhance drug's beneficial effect and improve its kinetic delivery, extending its retention time and activity in-situ, while reducing the toxicity and low dose-related inefficacy. Thermosensitive pNIPAM-based hydrogel and a GelMA-based light-sensitive hydrogel are under current synthesis and evaluation to develop an injecting and in-situ forming hydrogel solution. As regards tissue regeneration, vessel formation and a bacterial-free environment are key aspects to promote cellular proliferation and successful healing of the ablated tissue.We have internally developed a bottom-up protocol to synthesize naturally occurring ion-nanoparticles. These natural nanoparticles have a diameter at the nanoscale and have been encapsulated in PLA fiber, their applications in 2D tissue models have proved to be not toxic and their compositions have shown to be effective in terms of promoting cellular migration and sustaining ions' delivery at therapeutic concentration for almost 1 month.

POSTER 92 presented by:

NAME: Albert Ripoll

Colistin-loaded nanoparticles in combination with alginate lyases enhance *Pseudomonas aeruginosa*'s biofilm disruption

Albert Ripoll [1,2], Núria Blanco-Cabra [1,2], Raphaëlle Palau [1], Jose Carlos Ibáñez [3], Damien Lupin [3], Iraida Loinaz [3], Eduard Torrents [1,2]

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Pseudomonas aeruginosa biofilms are closely associated with persistent respiratory infections, particularly in chronic pulmonary diseases such as cystic fibrosis and chronic obstructive pulmonary disease (COPD), where they contribute to long-term inflammation and antibiotic tolerance. *P. aeruginosa* biofilms pose significant treatment challenges, particularly due to their dense extracellular matrix (ECM), which limits antibiotic penetration and contributes to drug tolerance. This study compares the antibiofilm efficacy of colistin, a cationic polymyxin, encapsulated in polymeric nanoparticles (KuDa-Col NPs), against free colistin (Col) in different *P. aeruginosa* strains biofilms grown under static (48 h) and dynamic (72 h) conditions. KuDa-Col NPs significantly improved biofilm biomass reduction and reduced its viability compared to free Col due to the charge masking effect provided by the nanoparticle. Moreover, KuDa-Col proved to retain free Col bactericidal potency in planktonic growth curve assays. Additionally, two alginate lyases were tested in combination with both free Col and KuDa-Col to disrupt the biofilm matrix and further improve antibiotic penetration and effectiveness. These combinations demonstrated synergistic or additive effects in reducing biofilm biomass and viability. These findings support the use of KuDa-col NPs and alginate lyase combinations as promising strategies to enhance Col penetration and efficacy in treating chronic *P. aeruginosa* biofilm infections.

POSTER 93 presented by:

NAME: Núria Blanco-Cabra

Galleria mellonella as a simple yet reliable *in vivo* model for nanotoxicology

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Nanomaterials are a rapidly advancing tool with applications across various scientific fields. However, their interactions with living organisms have raised numerous safety concerns, making it crucial to develop reliable models to predict and evaluate associated toxicity effects. Traditional *in vitro* assays fail to mimic the true physiological responses of living organisms to nanomaterials, whereas murine and other *in vivo* models are time-consuming, costly, and ethically controversial. The greater wax moth, *Galleria mellonella*, has emerged as a promising *in vivo* model for nanotoxicology, serving as an effective bridge between *in vitro* and *in vivo* mammalian testing. This model combines simplicity and ethical viability with a human-conserved innate immune system, making it ideal for immunotoxicity testing. While it cannot fully replace more complex animal models, *G. mellonella* represents a valuable alternative for early-stage nanotoxicity screening and deserves greater recognition and integration into toxicological research. However, despite its potential, the broader adoption of *G. mellonella* is currently limited by a lack of standardization and other methodological challenges.

POSTER 94 presented by:

NAME: Elena Muscolino

Nanomedicine for the treatment of Lafora disease: use of mRNA-loaded

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Lafora disease (LD) is an ultrarare and fatal autosomal recessive form of progressive myoclonus epilepsy. The disease affects apparently healthy teenagers and, due to the lack of effective treatments, inevitably leads to the death of patients 5-10 years after its onset. The hallmark of LD is the accumulation of cytoplasmic glycogen aggregates, known as Lafora bodies (LBs), in the brain and other tissues. LBs are a result of loss-of-function mutations in one of two genes: EPM2A, encoding laforin, or EPM2B, encoding malin. Both proteins are believed to form a functional complex that regulates key components of glycogen metabolism. Ultimately, as an autosomal recessive inherited single-gene disorder, LD is a good candidate for a gene therapy-based approach. Therefore, a possible treatment for LD would be the re-introduction of a functional copy of the mutated gene by means of gene therapy techniques. In this context, our work aims to use a new generation of polymers (poly-(beta amino-esters), pBAEs), ideal for gene replacement therapy thanks to their efficacy in encapsulating and protecting mRNA and selectively delivering it to target cells, where the codified protein is efficiently expressed. Various formulations of mRNA-loaded pBAEs have been generated and their cytotoxicities have been studied *in vitro*. pBAES carrying myc-tagged malin mRNA have been formulated and, following *in vitro* transfections, the expression of the malin protein has been assessed via western blotting. Intracerebral injections of GFP mRNA-loaded pBAEs into wild-type mice have been carried out to assess the brain biodistribution of the particles. Thus far, *in vitro* results have demonstrated the low cytotoxicity and high transfection efficiency of the particles. Malin mRNA-loaded pBAEs transfected cells *in vitro* and malin was successfully expressed. While the *in vivo* brain biodistribution of the particles has not yet been fully assessed, future work will focus on targeting the particles to specific cell types, namely neurons and astrocytes. Lastly, malin mRNA-loaded pBAEs will be administered to malin-deficient mice and their efficacy in ameliorating disease progression will be assessed. These future *in vivo* studies using malin-deficient mice will be crucial in determining the potential of our particles as a novel treatment strategy for LD and potentially other neurodegenerative diseases that may benefit from gene therapy.

POSTER NANOMEDICINE

POSTER 95 presented by:

NAME: Roger Fàbrega Alsina

The Physicochemical, biopharmaceutical, and *in vitro* efficacy properties of diclofenac-loaded liposomes

Roger Fàbrega Alsina, Iria Naveira Souto, Elisabet Rosell Vives, Ferran Roig Roig, Maria Lajarin Reinares, Josep Samitier i Martí, Jessica Malavia Muñoz, Anna Lagunas Targarona

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Diclofenac-loaded liposomes were developed as a tool to treat inflammatory skin disorders. Topical administration of this molecule is a challenge that can be addressed by encapsulation into drug delivery systems. The aim of the current study was to develop, purify and optimize the process to obtain Small Unilamellar Vesicles (SUVs) of 50-100 nm liposomes drug delivery system for the local administration of diclofenac. The physicochemical properties of SUVs were characterized using dynamic light scattering (DLS) to measure particle size, Z-potential, polydispersity index (PDI), and nanoparticle concentration. The encapsulation efficiency () was determined using HPLC-UV analysis, with a previous separation of free diclofenac from liposomes by centrifugation with ultrafiltration units. The *in vitro* permeation and release profiles were investigated with vertical diffusion Franz cells. Vesicles obtained (size, 86.43 ± 8.36 nm

POSTER 96 presented by:

NAME: Silvia Muro

Identification of an anti-ICAM-1 antibody for improved isoform-dependent targeting and transport across the blood-brain barrier

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Drug delivery to the brain is highly impaired by the blood-brain barrier (BBB). To overcome this problem, drugs and drug carriers are often targeted to endothelial receptors involved in BBB transcytosis. However, the fact that these receptors, as most body proteins, are not expressed in an exclusive configuration but as various isoforms has been long overlooked. Illustrating this paradigm, we focused on intercellular adhesion molecule 1 (ICAM-1), an endothelial receptor overexpressed in many pathologies. ICAM-1 has five extracellular domains (D1 to D5) that can be targeted, yet most prior targeting studies have used D2-specific antibody (Ab) R6.5. While this provides BBB transport in cellular models, literature suggests the presence of ICAM-1 isoforms lacking D2 (-D2 ICAM-1) *in vivo* in mice. In this study, we investigated for the first time the presence of -D2 ICAM-1 isoforms in human brain endothelial cells. Quantitative RT-PCR, Western blot, and radioimmunotracing revealed the abundant presence of-D2 ICAM-1 isoforms at both mRNA and protein levels. To study isoform-dependent targeting, we developed recombinant cells lines expressing -D2 ICAM-1 vs. full-length ICAM-1 and used them to compare the targeting efficiency of commercial anti-ICAM-1 Abs (15.2, R6.5, G-5, H4) and new Abs we developed using phage display (B4, B6, B11, C12, G2). One commercial (G-5) and two new (B4, B6) Abs were the best at targeting cells expressing-D2 ICAM-1 recombinantly (>2x1012 sum intensity\/ well, 15-fold above R6.5 control). They also induced uptake by endothelial cells expressing the full pool of ICAM-1 isoforms (40-80% NPs in 1 h). These Abs were coated on polymer nanoparticles (NPs) and the resulting formulations showed good targeting specificity (>10-fold vs. IgG NPs). Using BBB cell models with validated barrier function (presence of cell junctions and lack of NP leakage), these formulations exhibited efficient transcytosis across endothelial linings, with one of them, which was coated with Ab B4, being the best (95% transcytosis in 24 h). This study illustrates that the identification of both receptor isoforms expressed by the BBB and targeting antibodies capable of recognizing them holds great promise to improve brain targeting for drug delivery purposes.

POSTER | NANOMEDICINE

POSTER 97 presented by:

NAME: Ángela Martínez Mateos

DnaA acts as a transcriptional activator that regulates nrdAB ribonucleotide reductase expression in *Pseudomonas aeruginosa* PAO1

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Pseudomonas aeruginosa is a highly adaptable, opportunistic pathogen that exhibits both acquired and innate mechanisms of antibiotic resistance. Due to its ability to survive in various environments, discovering new therapeutic strategies is essential. Ribonucleotide reductases (RNRs), essential enzymes for dNTP synthesis, have become promising targets for fighting *P. aeruginosa* infections. There are three main RNR classes (I, II, III), each distinguished by how their radical is generated, the metal required, cofactor type, structure, and oxygen needs. *P. aeruginosa* encodes all three RNR classes in its genome and understanding them is crucial for comprehending its metabolic adaptability under different growth conditions, such as planktonic, during infection, or biofilm formation.

Pseudomonas aeruginosa is a highly adaptable, opportunistic pathogen that exhibits both acquired and innate mechanisms of antibiotic resistance. Due to its ability to survive in various environments, discovering new therapeutic strategies is essential. Ribonucleotide reductases (RNRs), essential enzymes for dNTP synthesis, have become promising targets for fighting *P. aeruginosa* infections. There are three main RNR classes (I, II, III), each distinguished by how their radical is generated, the metal required, cofactor type, structure, and oxygen needs. *P. aeruginosa* encodes all three RNR classes in its genome and understanding them is crucial for comprehending its metabolic adaptability under different growth conditions, such as planktonic, during infection, or biofilm formation.

Our laboratory previously found that class Ia (nrdAB) is positively regulated by AlgR, which controls mucoidy in *P. aeruginosa*, and negatively regulated by NrdR, the master repressor that controls all three classes of RNR. However, significant gaps remain in our understanding of the regulatory network of the class Ia RNR, and we don't fully understand which transcriptional regulators are involved in the fine-tuning of gene regulation for the different RNR classes.

This project aims to identify new transcriptional regulators through genomic, transcriptomic, and proteomic approaches. It has been suggested that DnaA, among other transcriptional regulators, could be involved in the regulation of these pathways. Comprehensive studies of these regulators are necessary to elucidate the complex regulatory networks and hierarchical organization of these factors. Understanding these interactions is crucial for developing effective strategies to combat *P. aeruginosa* infections.

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POSTER 98 presented by:

NAME: Carla Arroyo

Tiny Signals, Big Impact: Toward Personalized Monitoring of Cardiovascular Health

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Heart failure (HF) has been defined as a global pandemic, with 64.3 million people estimated to suffer from it worldwide in 2017 [1]. These figures, however, do not account for the vast number of patients who remain undiagnosed or are misdiagnosed, often due to the absence of continuous, personalized monitoring systems. Therefore, a point-of-care system capable of providing both patients and clinicians with relevant and accurate data on disease progression and severity could greatly enhance clinical decision-making and patient outcomes. In this context, the European project IV-Lab, aims to develop an implantable, multi-sensing device capable of detecting both hemodynamic and biochemical parameters related with early detection of HF. This work specifically focuses on the development of an electrochemical multiparametric array capable of estimating electrolytes in blood ($K+$ and $H+$) and, specific cardiac biomarkers (BNP and NT-proBNP). The sensors demonstrated high sensitivities, exceeding 95 mVV/mM for potassium and 90 mVV/pH for hydrogen ions. In addition, to overcome one of the main limitations of implantable sensors, such as their short useful life due to the sensor fouling as a reaction of the body to a foreign object, also we are evaluating the antifouling properties of a polymeric hydrogel coated onto the potassium sensor membrane to prevent coagulation and signal degradation. For the detection of specific biomarkers BNP and NT-proBNP, we are developing a novel configuration of electrochemical aptabeacon (APTB) to interact specifically with these biomarkers. The possible structural folds of the APTB have been computationally analysed and theoretical measurements of its base lengths have been made to ensure a suitable distance between the electrode and the redox molecule bound at 3' with the APTB. The characterization platform consists of an SPR system coupled with a potentiostat, enabling real-time kinetic monitoring of APTB-BNP interactions while simultaneously capturing potentiometric and amperometric data.

POSTER NANOMEDICINE

POSTER 99 presented by:

NAME: Daniel Gonzalez Carter

Endocytic Turnover of Endothelial Cell-Membrane Proteins as a Driver of Blood Brain Barrier Specialization and Dysfunction

Alba Tomás-Sitjes [1,2], Gianluca Arauz-Garofalo [2], Marina Gay [2], Sònia Jarió [2], Marta Vilaseca [2], Giuseppe Battaglia [1,3], Daniel Gonzalez-Carter [1]*
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The blood-brain barrier (BBB), formed primarily by specialized brain endothelial cells (BEC), exerts essential functions for proper brain activity, including nutrient transport, signal transduction, immune cell transmigration and pathogen restriction. While these functions are known to be regulated by the identity and abundance (i.e. composition) of cell-membrane proteins, a parameter which remains underexplored is how protein endocytic turnover rate (ETOR) - the rate of protein internalization from the cell membrane - governs BBB physiology. Employing high-throughput in vitro proteomics, we quantify the ETOR of large protein arrays (c. 1000 individual proteins) across endothelial phenotypes and pathological states to examine the mechanisms driving BBB specialization and the changes underlying BBB dysfunction. We find that BEC possess a specialized ETOR profile which differentiates them from peripheral endothelial cells beyond their cell membrane protein composition. In addition, we demonstrate that inflammatory conditions disrupt the endocytic rates of BEC to a greater degree than disruptions in protein abundance, shifting the specialized ETOR profile of BEC towards a peripheral phenotype. Furthermore, we find that, while inflammation-induced changes in protein abundance identify proteins strongly involved in immune response, inflammation-induced changes in ETOR identify proteins strongly involved in vasculature remodelling. Together, our results indicate that the endocytic turnover of cell membrane proteins is an important parameter driving the specialization of the BBB which becomes disrupted during pathological conditions independently of cell membrane protein composition. Furthermore, it highlights that ETOR changes underly inflammatory responses not modulated by changes in protein abundance.

POSTER 100 presented by:

NAME: Gender Comission

Promoting Gender Equality, Diversity, and Inclusion at IBEC: Goals and Actions of the Gender and Diversity Commission

IBEC

At the Institute for Bioengineering of Catalonia (IBEC), we believe that excellence in research and a healthy working environment can only be achieved by embracing equality, diversity, and inclusion. The Gender and Diversity Commission works to ensure that all individuals—regardless of gender, age, sexual orientation, nationality, or ability—feel valued, represented, and empowered.

In 2024, we launched the , Diversity, Equity, and Inclusion (DEI) Plan (2024–2028), which guides our efforts across leadership, recruitment, career progression, work-life balance, and inclusive research. Over the last year, we have taken concrete steps to embed GDEI principles into IBEC's culture and operations.

Some of the key actions implemented so far are:

• Leadership evaluation: added a GDEI indicator to Group Leaders' performance reviews.

• Role model visibility: co-hosted "Picture a Scientist" screening with IRB and PCB, featuring diverse leaders and early-career researchers.

• Inclusive recruitment: delivered training on competency-based recruitment with a gender and diversity lens.

• Book Club: launched a G&D-focused book club to foster reflection and dialogue.

• LGTBIAQ+ Inclusion Plan: developing updated measures through focus groups and surveys.

• Onboarding: introduced G&D resources in welcome sessions for new staff.

• Training: offered sessions on gender, diversity, equity, and inclusion.

• Communities of Practice (CoP): Engaged with networks such as Hipatia, SOOMA, CERCA, and INSPIRE.

• Gender Analysis in Research: conducted a study on gender representation in publications, highlighting ongoing disparities.

• Integration of Gender in Research: conducted a survey amongst group leaders to analyse how IBEC research groups are integrating gender at their research.

Through these initiatives, we aim to drive lasting cultural and structural change, ensuring that IBEC is a place where everyone can thrive and contribute to scientific excellence.

IBEC

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