20 YEARS IBEC

Institute for Bioengineering of Catalonia

IBEC
20th Anniversary Symposium

OCTOBER 22nd AND 23rd, 2026
BARCELONA

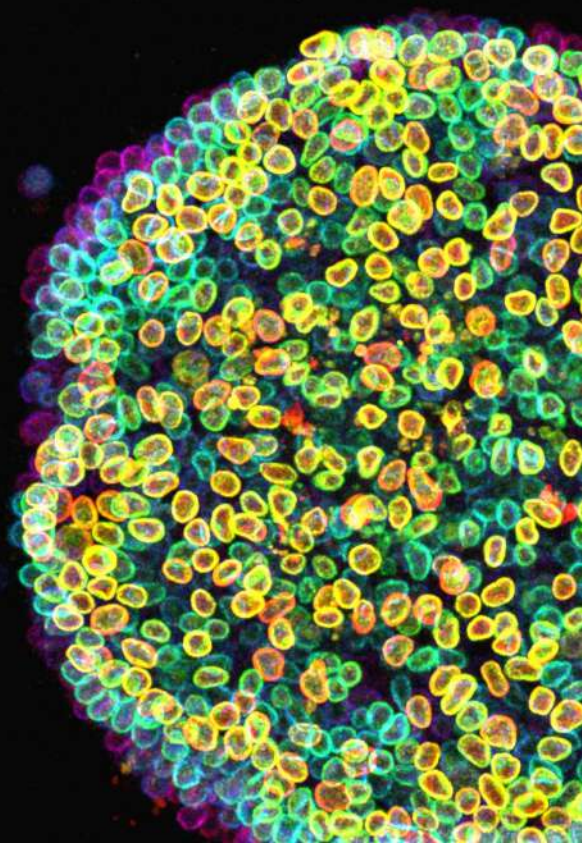


Image credit: Özge Özgüç, Integrative Cell and Tissue Dynamics Research Group.

Designed and produced by the
Communications Office of the Institute for Bioengineering of Catalonia

www.ibecbarcelona.eu

20 YEARS IBEC
Institute for Bioengineering of Catalonia

EXCELENCIA SEVERO OCHOA 2024-2028

Contents

Programme 4

Keynote Lectures 6

- Molly Stevens 8
- M. Ángela Nieto 10
- Li Tang 12

Flash Presentations 14

- Session 1 16
- Session 2 17
- Session 3 18

Posters 20

- Advanced microscopy 22
- Advanced therapeutic systems 23
- Biomodels and tissue engineering 25
- Mechanobiology 29
- Smart data analysis 31
- Additional posters 32

Abstracts 33

- Advanced microscopy 33
- Advanced therapeutic systems 44
- Biomodels and tissue engineering 76
- Mechanobiology 130
- Smart data analysis 158
- Additional posters 173

20 YEARS IBEC
Institute for Bioengineering of Catalonia

20th Anniversary

IBEC Symposium

October 22nd and 23rd · Barcelona

Programme

Thursday 22nd October

World Trade Center Barcelona

08:15 – 09:00	Registration
09:00 – 09:15	Opening ceremony
09:15 – 09:40	*Director's presentation* **Manuel Salmerón**, Director IBEC
09:40 – 10:25	**Molly Stevens** · University of Oxford Designing and translating next generation biomaterials for disease detection and therapeutics
10:25 – 11:00	**Flash presentations. Session 1**
11:00 – 11:45	Coffee break
11:45 – 12:25	**Ángela Nieto** · Instituto de Neurociencias CSIC-UMH Cancer cell plasticity trajectories from primary tumors to metastatic outgrowths
12:25 – 13:10	**Flash presentations. Session 2**
13:10 – 13:30	PhD Award
13:30 – 14:45	Lunch break

14:45 – 15:25	**Li Tang** · EPFL Multidimensional immunoengineering to advance cancer immunotherapy: the journey from bench to bedside and back
15:25 – 16:10	**Flash presentations. Session 3**
16:10 – 16:45	Thematic Networks
16:45 – 16:50	**Ece Kutukcu** · PhD Committee
16:50 – 17:00	**Awards and closing ceremony** PhD Certificate of Excellence Best Flash Talk
17:00 – 18:00	20th Anniversary celebration toast

Friday 23rd October

Sant Pau Recinte Modernista

10:00 – 12:30	Poster Session


IBEC



Keynote Lectures

Thursday 22nd October · 9:40 h

KEYNOTE LECTURE

Designing and Translating next generation biomaterials for disease detection and therapeutics

Stevens, Molly
University of Oxford, United Kingdom

This talk will provide an overview of recent advances in materials for therapeutic and biosensing applications, with a particular focus on establishing translational pipelines to bring our innovations to the clinic [1]. We have developed fabrication methods to engineer complex 3D architectures and biofunctionalized surfaces, incorporating spatially arranged bioinstructive biochemical and topographical cues [2]. Our therapeutic delivery portfolio includes high-molecular-weight polymer carriers for enhanced delivery of saRNA therapeutics, as well as photo-responsive nanoreactors inspired by circadian rhythms [3]. Additionally, we are developing innovative solutions for targeted and controlled delivery using soft robotics with unique bioinspired properties that respond to external stimuli to release therapeutic payloads [4]. Our design approach integrates state-of-the-art fabrication techniques while prioritizing versatility and scalability to maximize translational potential. We are exploiting the new sensing capabilities such as functionalised nanoparticles to engineer nanoprobes for in vivo disease diagnostics that produce a colorimetric response ideal for naked eye read-out, for CRISPR-based preamplification free detection of ncRNAs (CrisprZyme) and quantum biosensing [5]. Additional work explores alternative synthetic binders that can be incorporated into both diagnostic and therapeutic systems to enhance molecular recognition of cancer targets [6]. Furthermore, we have developed Raman microspectroscopy imaging tools and machine learning algorithms for hyperspectral unmixing of complex biological imaging. These technologies enable us to investigate live-cell and organoid models and visualize the in vivo fate of nanomedicines [7]. I will present recent advances in Raman spectroscopy for high-throughput, label-free characterization of single nanoparticles—an approach we pioneered through the SPARTA™ technique—which allows for the comprehensive analysis of a broad range of nanoparticle-based therapeutics and exosome-based diagnostics [8]. Finally, I will explore how these versatile technologies can drive transformative biomedical innovations. I will also discuss our efforts in establishing effective translational pipelines to accelerate clinical applications while actively working towards the democratization of healthcare [9].

[1] J. P. K. Armstrong... M. M. Stevens. "A blueprint for translational regenerative medicine." Science Translational Medicine. 2020. 12(572): eaaz2253.; C. S. Wood, ... M. M. Stevens. Nature. 2019. 566: 467-474.; C. N. Loynachan, ... M. M. Stevens. Nature Nanotechnology. 2019. 14: 883–890.

[2] T. von Erlach, ... M. M. Stevens. Nature Materials. 2018. 17: 237-242; C. Chiappini... M. M. Stevens, E. Tasciotti. Nature Materials. 2015. 14: 532.

[3] A. Najer, ... M.M. Stevens. ACS Central Science. 2022. 8(9): 1238–1257; [3] A. Blakney, ... M. M. Stevens. ACS Nano. 2020, 14(5): 5711-5727; O. Rifaie-Graham, ... M.M. Stevens. Nature Chemistry. 2023. 15: 110–118.

[4] X. Song... M. M. Stevens. Advance Materials. 2022. 34(43): 2204791.; R. Sun... M. M. Stevens. Advanced Materials. 2022. 35(13):2207791.

[5] C. N. Loynachan, ... M. M. Stevens. Nature Nanotechnology. 2019. 14: 883-890; M. Broto, ... M. M. Stevens. Nature Nanotechnology. 2022. 10: 1038.; A. Lo Fiego,...M. M. Stevens. Nature Reviews Physics. 2025. 7:672–674.

[6] C. Sadler, ..., M.M. Stevens. JACS (2025) https://doi.org/10.1021/jacs.4c17452

[7] C. Kallepitis, ... M. M. Stevens. Nature Communications. 2017. 8: 14843. D. Georgiev, ... M. M. Stevens, M. Barahona. PNAS. 2024. DOI: 10.1073/pnas.2407439121.

[8] J. Penders, ... M. M. Stevens. Nature Communications. 2018, 9: 4256.; J. Penders, ... M. M. Stevens. ACS Nano. 2021, 15, 11, 18192–18205; H. Barriga, ... M. M. Stevens. Advanced Materials. 2021, 34(26):2200839.

[9] A. T. Speidel, ... M. M. Stevens. Nature Materials. 2022. DOI: 10.1038/s41563-022-01348-5.



Stevens, Molly
University of Oxford, United Kingdom

Professor Dame Molly Stevens FREng FRS is John Black Professor of Bionanoscience at the University of Oxford and Deputy Director of the Kavli Institute for Nanoscience Discovery. An internationally recognised leader in bionanoscience, her research spans biosensing technologies, regenerative medicine, biomaterials, and advanced therapeutics. She has published over 400 scientific papers, founded multiple spin-out companies, and received numerous prestigious awards. A Fellow of both the Royal Society and the Royal Academy of Engineering, she is renowned for pioneering innovations that bridge nanotechnology and healthcare.

Thursday 22nd October · 11:45 h

KEYNOTE LECTURE

Cancer Cell Plasticity Trajectories from Primary Tumors to Metastatic Outgrowths

Nieto, M. Ángela
Instituto de Neurociencias (CSIC-UMH), Alicante, Spain

Cellular plasticity is essential during embryonic development, when cells undergo profound changes in identity and behaviour to shape tissues and organs. In adult tissues, these processes are tightly regulated, but their aberrant reactivation can contribute to devastating diseases. Our work has revealed how distinct epithelial-to-mesenchymal transition (EMT) programmes, are deployed in different biological settings, including embryos, fibrosis and cancer.

In cancer, EMT-associated plasticity contributes to the generation of intratumoral heterogeneity by enabling cancer cells to lose their differentiated state and adopt distinct cellular trajectories. These trajectories recapitulate embryonic-like and adult fibrotic-like programmes, with opposing consequences for tumour progression: one promotes invasive behaviour and metastatic dissemination, whereas the other favours anti-tumour inflammation. These findings establish that EMT is not a single, uniform programme in cancer, but a source of divergent cell states that can shape the tumour ecosystem and disease evolution.

Building on this framework, we have investigated the metastatic potential of invasive cancer cells and extended their characterization to circulating tumour cells (CTCs) and metastatic outgrowths. Our findings reveal that invasive potential and the ability to establish metastases are distinct properties and indicate that metastatic competence is already shaped within the primary tumour, while cancer cells retain substantial plasticity at metastatic sites. Altogether, our findings illustrate how cellular plasticity programmes operating across developmental and pathological contexts provide a framework for understanding disease progression and identifying new therapeutic opportunities in cancer, fibrosis and organ degeneration.



Nieto, M. Ángela

Instituto de Neurociencias (CSIC-UMH), Alicante, Spain

Prof. Ángela Nieto is a Research Professor at the Institute of Neurosciences (CSIC-UMH) in Alicante and coordinator of the Cancer-CSIC Network. An internationally recognized leader in developmental biology, her research focuses on cellular plasticity during embryonic development and disease, particularly the role of embryonic programs in cancer progression, fibrosis, and bone formation. A member of EMBO and several national and international academies of science, she has received numerous prestigious distinctions, including the Rey Jaime I Award, the Ramón y Cajal National Research Award, and the L'Oréal-UNESCO For Women in Science Award. Her work has had a profound impact on our understanding of the links between development and human disease.

Thursday 22nd October · 14:45 h

KEYNOTE LECTURE

Multidimensional Immunoengineering to Advance Cancer Immunotherapy: The Journey from Bench to Bedside and Back

Tang, Li
Institute of Bioengineering, École polytechnique fédérale de Lausanne (EPFL), Switzerland

Our immune system interacts with many diseases in a multidimensional manner involving substantial biological, chemical, and physical exchanges. Manipulating the disease-immunity interactions may afford novel immunotherapies to better treat diseases such as cancer, an emerging field termed 'immunoengineering'. My lab aims to develop novel strategies to engineer the multidimensional immunity-disease interactions to create safe and effective therapies against cancer. We leverage the power of metabolic and cellular bioengineering, synthetic chemistry and material engineering, and mechanical engineering to achieve controllable modulation of immune responses. In this talk, I will first discuss our discovery of a new type of immune checkpoint with mechanical basis that is distinct from most known immune checkpoints of biochemical traits. We further developed novel interventions to overcome the mechanical immune checkpoint for enhanced cancer immunotherapy. Next, I will talk about our recent discovery of IL-10 and IL-4, type 2 immune function-related cytokines, as metabolic reprogramming agents that reinvigorate the terminally exhausted $CD8^+$ tumor infiltrating lymphocytes. This strategy has been extended to developing metabolically armored CAR-T cells with IL-10 secretion to counter exhaustion-associated dysfunction in the tumor microenvironment for enhanced anticancer immunity. This new CAR-T cell therapy, i.e. IL-10-secreting CAR-T, has shown promise in several on-going IIT clinical trials (NCT06393335, NCT05715606, NCT05747157, NCT06120166, NCT06277011) in the treatment of refractory/relapsed $CD19^+$ B cell leukemia and lymphoma, and lupus.



Tang, Li

Institute of Bioengineering, École polytechnique fédérale de Lausanne (EPFL), Switzerland

Li Tang is an Associate Professor at EPFL's Institute of Bioengineering, Switzerland, where he also serves as Vice Dean for Innovation at the School of Life Sciences and is Co-Founder & Chairman of Leman Biotech. He received his B.S. in Chemistry from Peking University, China, in 2007, and Ph.D. in Materials Science and Engineering from University of Illinois at Urbana-Champaign, USA, in 2012. He was a CRI Irvington Postdoctoral Fellow in the laboratory of Prof. Darrell Irvine at Massachusetts Institute of Technology during 2013-2016. He joined the faculty of Institute of Bioengineering, and Institute of Materials Science & Engineering, at École polytechnique fédérale de Lausanne (EPFL), Switzerland, as a Tenure-Track Assistant Professor in 2016, and promoted to Associate Professor with tenure in 2022. His research focuses on multidimensional immunoengineering to advance cancer immunotherapies. Prof. Tang has received many prestigious awards, including the ERC Consolidator Grant (2025) and Starting Grant (2018), Biomaterials Award for Young Investigators (2024), Biomaterials Science Lectureship (2025), Leenaards Prize for Translational Medical Research (2025), Friedrich Miescher Award (2025), and Lem Prize (2025), and was named to Clarivate Highly Cited Researcher (2025), and MIT Technology Review's "Top 35 Innovators Under 35" in China (2020).




FLASH Presentations

FLASH PRESENTATIONS · SESSION 1

Thursday 22nd October · 10:25 – 11:00 h

NAME	SURNAME	TITLE
Mauricio	Cano Galván	Mechanotool: An Autonomous Open-Source Software Platform for Large-Scale Multiparametric Analysis of Bio-Atomic Force Microscopy data
Zahra	Saeidikia	Imaging and modelling PEG-PLA nanoparticles and their disassembly of Aβ42 fibrils
Esteban	Suárez Baquero	Development of an All-Optical Platform for Imaging and Holographic Manipulation of Neural Circuits in Behaving Mice
Fleur	Clemenceau	Simultaneous 12-lead ECG for the validation of novel cellulose-based electrodes in human subjects
Lluís	Fernández Romero	Curvature Regularized Time Warping for Chromatographic Alignment
Mariano	Martín	Systematic mutational mapping reveals optimal amyloid formation for RIPK function
Revathi	Ravindran	Towards a Comprehensive Modelling and Design Framework for Predicting Biodegradation at a Macroscale

FLASH PRESENTATIONS · SESSION 2

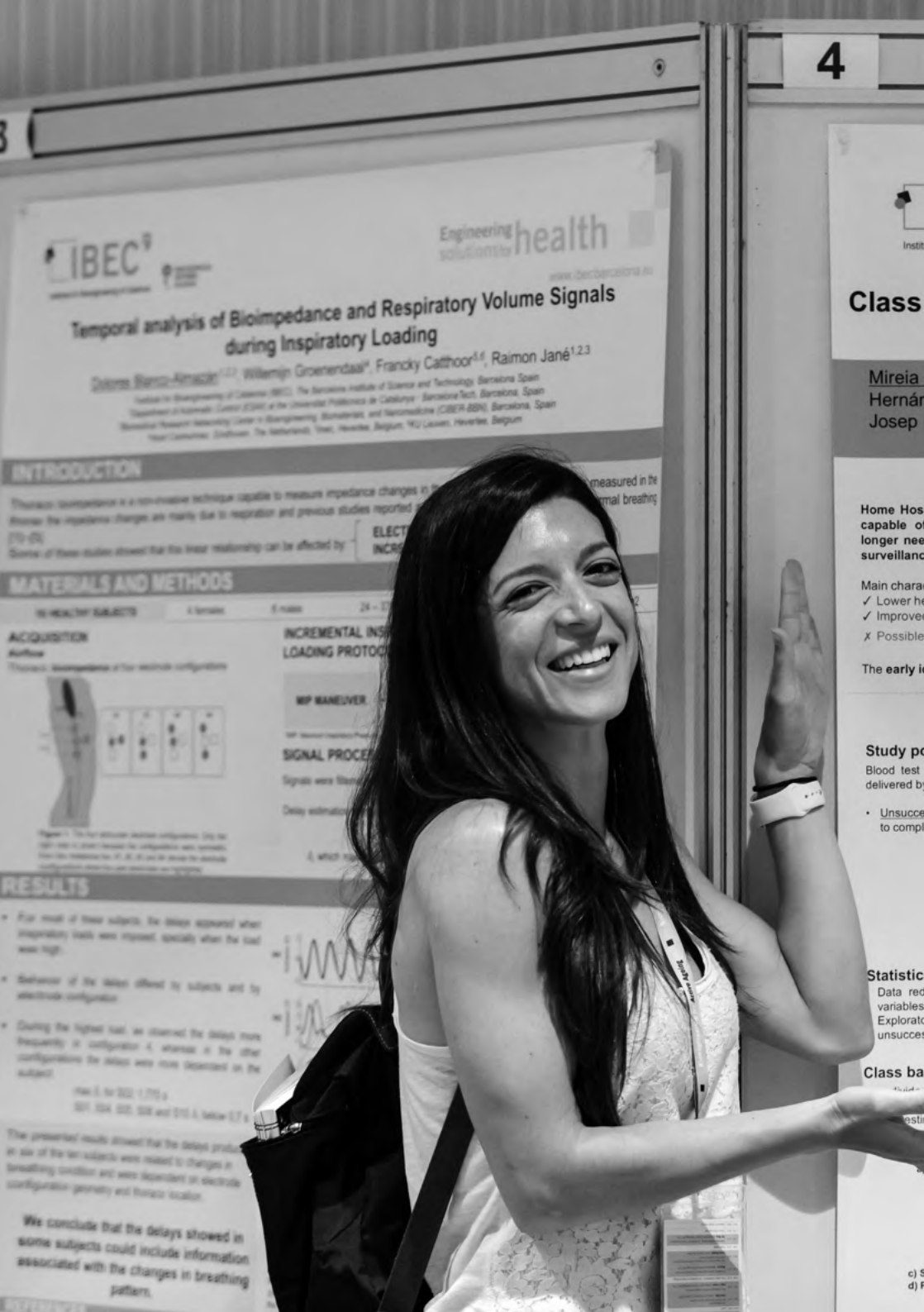
Thursday 22nd October · 12:25 – 13:10 h

NAME	SURNAME	TITLE
Joel	Àlvarez Puig	Modelling biomaterial-associated biofilm infections in *Galleria mellonella* for antibiotic susceptibility screening
David	Bartolomé Català	Microphysiological reconstruction of the colonic tumor microenvironment for T cell migration studies
Florencia	Lezcano	Toward biohybrid facial actuation: 3D bioprinting of functional skeletal muscle systems
Andreu	Matamoros Anglès	Extracellular vesicles in Alzheimer's disease: Amyloid β aggregation and neuronal network dysfunction
Nicolle	Miranda de Lima	Engineering a Scalable and Highly Sensitive Microfluidic Platform for Real-Time Hyperpolarised 13C Metabolic Imaging of 3D Hepatoblastoma Models
Daniel	Moya Rull	A reproducible and scalable human airway and lung organoid platform for infection modelling and therapeutic screening
Chiara	Ninfali	A Human 3D Platform combining Engineered Skeletal Muscle and Pancreatic Cancer Spheroids to model Cancer-Associated Cachexia
Anna	Panteleeva	Monitoring Neurodegeneration in a Brain-on-a-Chip with an NfL Biosensor
Francisco Manuel	Sáez González	From Organoids to Assembloids: Modeling Neurovascular Dynamics in Spinal Cord Injury
Jarmila	Stankova	Spatially resolved analysis of CRISPR-mediated metabolic gene knockouts in tumor xenografts

FLASH PRESENTATIONS · SESSION 3

Thursday 22nd October · 15:25 – 16:10 h

NAME	SURNAME	TITLE
Claudia	Camarero-Hoyos	A multifaceted approach to define a novel family of antimalarial compounds: the role of protein aggregation in *Plasmodium*.
Dario	Castellana	Dual-Action 3D Biomaterial for radiotherapy: protection and regeneration of tissue during X-ray treatment
Esra	Kasapgil	Endothelium-mimicking hemocompatible coatings for artificial placenta systems
Joaquín	Martínez Tambella	Restoration of edge detection and visually guided behavior in ambient white light with photoswitchable small molecules
Carlos	Moreno Yruela	Nucleosome-Based Platforms to Decipher Histone Deacetylase Mechanisms and Develop Modulators in High Throughput
Aina	Albajar Sigalés	Studying the mechanical regulation of nucleocytoplasmic transport using Single Molecule Tracking
Mariana	Azevedo Gonzalez Oliva	Soft matrix viscoelasticity: from mechanotransduction to neural communication
Marija	Matejčić	Mechanical Coordination of Intestinal Cell Extrusion by Supracellular 3D Force Patterns
Laura	Parra Gutiérrez	Characterization of matrix invasion and monolayer formation during early mouse embryo implantation


4
IBEC
Engineering solutions for health
Temporal analysis of Bioimpedance and Respiratory Volume Signals during Inspiratory Loading
INTRODUCTION
MATERIALS AND METHODS
RESULTS
We conclude that the delays showed in some subjects could include information associated with the changes in breathing pattern.
Class
Mireia
Hernán
Josep
Home Hos
capable o
longer nee
surveillanc
Main chara
✓ Lower he
✓ Improve
✗ Possible
The early i
Study po
Blood test
delivered b
Unsucce
to compl
Statistic
Data rec
variables
Explorato
unsucces
Class ba

IBEC
ute for Bioengineering of Catalonia

EXCELENCIA SEVERO OCHOA

Engineering solutions for health

www.ibecbarcelona.eu

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
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
Hospital Clínic de Barcelona (Spain), between 2012 and 2015.

ssful 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 ± 14.7	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%)	0.276
Acute	569 (30.8%)	28 (27.7%)	0.594

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

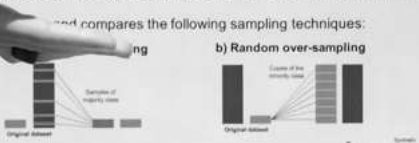
al analysis

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

lancing

ining (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.

nd compares the following sampling techniques:



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



Results

Correlation analysis

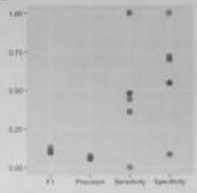
- **Hematocrit** was positively correlated with both **hemoglobin concentration** ($\rho = 0.98$) and **red blood cell count** ($\rho = 0.91$).
- Percentage and total amount of **neutrophils** ($\rho = -0.97$) and **lymphocytes** ($\rho = 0.96$) were highly correlated.

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 *Sensitvity*: 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	Mauricio	Cano Galván	Mechanotool: An Autonomous Open-Source Software Platform for Large-Scale Multiparametric Analysis of Bio-Atomic Force Microscopy data
2	Zahra	Saeidikia	Imaging and modelling PEG-PLA nanoparticles and their disassembly of Aβ42 fibrils
3	Esteban	Suárez Baquero	Development of an All-Optical Platform for Imaging and Holographic Manipulation of Neural Circuits in Behaving Mice
4	Belle	Clayton	Uncovering the Transcriptional Regulation of Ribonucleotide Reductases in *Pseudomonas aeruginosa*
5	Courtney Christine	Hospes	2-Photon Imaging and Manipulation of Memory Circuits in Freely Moving Mice
6	Gonzalo	Alonso Reillo	Metabolic Analysis in real time by using benchtop NMR Technology
7	Jhon	Pazos	Enhanced Scanning Dielectric Microscopy: On-Resonance operation for improved signal-to-noise ratio in nanoscale dielectric characterization
8	Raquel	García Olivas	Microscopy Characterization Facility: Enabling Advanced and Quantitative Imaging
9	Sepideh	Sadat Mirhosseini	Development of a Two-Photon Holographic Mesoscope for Large-Scale Optogenetic Stimulation with Single-Cell Resolution
10	Tom	White	Pathogenic collagen VI variants impair extracellular matrix mechanics at the nanoscale
11	Yoel	Melul Steinfeld	A Closed-Loop System for Real-Time Calcium Imaging, Neuron Selection, and Targeted Photostimulation in Freely Moving Mice

N	NAME	SURNAME	TITLE
12	Claudia	Camarero-Hoyos	A multifaceted approach to define a novel family of antimalarial compounds: the role of protein aggregation in *Plasmodium*.
13	Dario	Castellana	Dual-Action 3D Biomaterial for radiotherapy: protection and regeneration of tissue during X-ray treatment
14	Esra	Kasapgil	Endothelium-mimicking hemocompatible coatings for artificial placenta systems
15	Joaquín	Martínez Tambella	Restoration of edge detection and visually guided behavior in ambient white light with photoswitchable small molecules
16	Carlos	Moreno Yruela	Nucleosome-Based Platforms to Decipher Histone Deacetylase Mechanisms and Develop Modulators in High Throughput
17	Adriano	Caliari	Engineering superselectivity in a synthetic endocytosis model
18	Ainhoa	González Caelles	Photomechanical Vapor Nanobubble Engineering of Whole-Cell Vaccines for Bladder Cancer Prophylaxis
19	Albert	Ripoll	Novel Alginate Lyases Enhance Antibiotic Efficacy Through Biofilm Matrix Disruption in *Pseudomonas aeruginosa*
20	Albert	Ripoll	Enhanced Colistin Penetration Through Nanoparticle Encapsulation and Biofilm-Dispersing Enzymes to Treat Chronic Bacterial Infections
21	Alice	Lissmatz	Mapping the mutational landscape of Gelsolin D2 amyloid aggregation
22	Anna	Griego	An AUTOTAC-Inspired Nanoparticle Strategy to Promote Host-Driven Clearance of *Pseudomonas aeruginosa*
23	Carles	Prado Morales	SkinBots for the topical delivery of antigens
24	Carles	Verdaguer	Developing a multicellular 3D *in vitro* model for the detection of high-performing iPSC-derived CAR-NK against HER2+ solid tumors
25	Daniela	Currea	Unravelling the Molecular Targets and Mode of Action of Compound EMA377 in *Leishmania infantum*
26	Dayaneth	Jácome Montero	From Brain to Blood: Evaluation of miR-519a-3p as a Minimally Invasive Biomarker for Alzheimer's Disease

N	NAME	SURNAME	TITLE
27	Dunja	Arsenijevic	Exploring the interactions of small-molecule probes with protein condensates as a potential targeting mechanism in *Plasmodium falciparum*
28	Guanyu	Zhou	Engineering Multivalent ApoE Nanostructures for Isoform-Dependent Neurovascular Unit Reprogramming
29	Ilaria	Porello	Phosphorylcholine-presenting polymer micelles with intrinsic anti-inflammatory activity via scavenger receptor engagement
30	Inés	Macías Tarrío	Nanomotors-mediated delivery of FGFR3 inhibitor for bladder cancer therapy
31	Kristin	Fichna	Nanomotor-Driven Transport Potentiates ADC Efficacy Across Target Heterogeneity
32	Lucia	Roman	YAT2150 Analogues Target Stress-Induced Molecular Condensates in *Leishmania infantum*
33	Marta	Badia Graset	Mapping distinct Aβ42 aggregation pathways for precision medicine
34	Martín	Ruiz Gutiérrez	Portable grating-coupled SPR platform using Blu-ray-based sensing chips for multiplexed biosensing
35	Núria	Blanco-Cabra	A simple diagnostic platform reveals shear stress as critical in biofilm development.
36	Samantha	Morón Ros	3D-Bioprinting of functional β-cell spheroids for Type 1 Diabetes treatment
37	Sarahi	Elizondo	Ionicombisomes: Synthetic Cells Across Mucus
38	Sergi	Tosal	PolyQ expansion remodels the sequence determinants of huntingtin nucleation
39	Tomás	Quiroga	The folding, dimerization and allosteric landscapes of the ALS protein SOD1: a comprehensive mutational atlas
40	Yaiza	Andrés	Deep Mutational Scanning of Tau Amyloid Nucleation
41	Yasaman	Keshmiri	Tandem Enzymatic Activity of Catalase- and Glucose Oxidase- powered Nanomotors for Oxygen Generation and Therapeutic Modulation in Inflammatory Bowel Disease

N	NAME	SURNAME	TITLE
42	Joel	Àlvarez Puig	Modelling biomaterial-associated biofilm infections in *Galleria mellonella* for antibiotic susceptibility screening
43	David	Bartolomé Català	Microphysiological reconstruction of the colonic tumor microenvironment for T cell migration studies
44	Florencia	Lezcano	Toward biohybrid facial actuation: 3D bioprinting of functional skeletal muscle systems
45	Andreu	Matamoros Anglès	Extracellular vesicles in Alzheimer's disease: Amyloid β aggregation and neuronal network dysfunction
46	Nicolle	Miranda de Lima	Engineering a Scalable and Highly Sensitive Microfluidic Platform for Real-Time Hyperpolarised 13C Metabolic Imaging of 3D Hepatoblastoma Models
47	Chiara	Ninfali	A Human 3D Platform combining Engineered Skeletal Muscle and Pancreatic Cancer Spheroids to model Cancer-Associated Cachexia
48	Anna	Panteleeva	Monitoring Neurodegeneration in a Brain-on-a-Chip with an NfL Biosensor
49	Francisco Manuel	Sáez González	From Organoids to Assembloids: Modeling Neurovascular Dynamics in Spinal Cord Injury
50	Jarmila	Stankova	Spatially resolved analysis of CRISPR-mediated metabolic gene knockouts in tumor xenografts
51	Agnieszka	Nikitiuk	Beyond the Cell: Engineering the HPV-Negative HNSCC Microenvironment for Matrix-Dependent Drug Screening
52	Ainoa	Tejedera-Villafranca	Modeling Duchenne Muscular Dystrophy Cardiomyopathy Using hiPSC-Derived 3D Cardiac Co-Cultures
53	Alba	Calonge Sanz	Optimization of Calu-3 and primary bronchial epithelial cell (PBEC) air-liquid interface (ALI) models for investigating chronic *Pseudomonas aeruginosa* respiratory infections.
54	Angela M.	Ramírez Rosales	Nanocellulose & Bacterial Cellulose for Medical and Environmental Applications
55	Anna	Vilche Mariscal	Tuning Hydrogel Network Architecture in PEG–HA-Norbornene Hydrogels Enhances Brain Organoid Diffusion and Maturation
56	Carla	Arroyo	Optimization of the Blocking Step for Label-Free prism SPR Detection of C5b-9 in Human Serum as a Biomarker of Neuromuscular Junction Damage in Myasthenia Gravis

N	NAME	SURNAME	TITLE
57	Carolina	Tarantino	Modeling Ataxia-Telangiectasia Neurodevelopment Using an Optimized Isogenic Human Cerebral Organoid Platform
58	Davide	Arena	A Modular “Click” Hydrogel Platform for 3D Cell Culture and High-Throughput Screening
59	Ece	Kutukcu	Influence of Mechanical Stimulation and Matrix Stiffness on Breast Cancer Cells
60	Eduard	Torrents	Polymicrobial Interactions Involving *Burkholderia cenocepacia* Enhance Virulence, Alter Host Responses, and Modulate Antibiotic Tolerance in Cystic Fibrosis Infection Models
61	Emma	Oriol	Two-photon polymerized anisotropic microarchitectures for cardiomyocyte guidance
62	Eulàlia	Dou	From Prototypes to Production: A Scalable Blood–Brain Barrier-on-a-Chip for Pharmaceutical Screening
63	Eva	Garrido	Engineered Human Spinal Cord Constructs using 3D-bioprinting Technologies and iPSC-Derived Cells
64	Gal·la	Vinyes i Bassols	Glycocalyx remodeling at the blood-brain barrier: a microfluidic murine model to study cell-membrane protein endocytic dynamics
65	Inass	Himmiche	Ocular mechanism with embedded visual sensing for biohybrid robotics
66	Inés	Martínez Soria	Modulation of Hippocampal Vulnerability and Synaptic Plasticity by Adgrd1/GPR133 in Adult Mice
67	Jakub	Podraza	Integrating Microphysiological Systems and Longitudinal HP-MRI in Ovarian Cancer Modeling
68	Johannes	Gschwind	Generation and characterization of SALL1 and GATA3 knock-out human pluripotent stem cell lines for studying kidney development and disease
69	Jose	Huguet	Development of Barrier-Free Cancer-on-Chip Microfluidic Platforms for Studying the Cancer-Immunity Cycle in Colorectal Cancer
70	Júlia	Fabà Costa	An *ex utero* embryo culture platform to address peri-implantation development
71	Keerthy	Reghunandanan	Dissecting chemokine driven cell migratory behaviour of breast cancer in 3D Micro physiological system using a custom developed migration tracker

N	NAME	SURNAME	TITLE
72	Lluís	Mangas Florencio	Hyperpolarised 13C NMR enables functional drug response assessment in early-stage oncology drug development
73	Marc	Riu-Villanueva	An assembloid model to interrogate the contribution of inhibitory cortical interneurons to familial Alzheimer's disease network alterations
74	Maria	Escolà	Targeting nucleotide metabolism to attenuate *Pseudomonas aeruginosa* virulence
75	Marina	Rovira	Engineered Biohybrid Sphincter with Aperture Control
76	Marta	Ardèvol Teijelo	In situ Bioprinting: 6 DOF robotic system for advanced tissue engineering. Printing directly onto curved, non-planar anatomical surfaces
77	Michela	Lain Contato	Three-dimensional spheroid model of colorectal cancer cells in different metabolic conditions
78	Natalia	Castro	Development of personalized bioinks for skeletal muscle tissue engineering to understand the role of ECM in Duchenne muscular dystrophy
79	Nicola	Manicardi	Examining How Mfsd2a-Mediated Lipid Transport Regulates BBB Endocytic Dynamics
80	Oscar	España Romera	Spatial features of antigen escape in a CAR-T treated murine model of melanoma
81	Palash	Chandravanshi	Modelling Human Spinal Cord Injury and Repair in a 3D-Printed Organoid-on-a-Chip Device
82	Paulina Teresa	Sobierajska	Role of Amorphicity in Determining the Structure, Morphology, Thermal Stability and *In Vitro* Biological Response of Calcium Phosphates
83	Petra	Bauzon	Linking sarcolemmal instability to metabolic dysregulation: a DMD-on-Chip Platform investigating mitochondrial dysfunctions
84	Pol	Picón Pagès	Structural and Mechanistic Insights into GPR133 Signaling in Glioblastoma Multiforme
85	Rita	Grimalt Mirada	A Microengineered Platform for the Generation of Single-Lumen Human Spinal Cord Organoids
86	Thomas	Wilson	Epifluidics: a scaffold-free platform for perfusable, geometrically programmable, epithelial tubes

N	NAME	SURNAME	TITLE
87	Timothée	Caboche	A Magnetic Actuator-Based Platform for Functional Assessment of 3D Human Skeletal Muscle Bioengineered Tissues in Myotonic Dystrophy
88	Tobias	Walther	DNA hydrogel microparticles as phantom cells for tissue engineering
89	Vicent	Ribas Serra	Sex- and model-dependent hepatic pyruvate flux alterations in obesity revealed by HP-^{13}C NMR
90	Xavier	Barceló	Placenta-Derived ECM as a Spinal Cord-Mimetic Biomaterial

N	NAME	SURNAME	TITLE
91	Aina	Albajar Sigalés	Studying the mechanical regulation of nucleocytoplasmic transport using Single Molecule Tracking
92	Laura	Parra Gutiérrez	Characterization of matrix invasion and monolayer formation during early mouse embryo implantation
93	Àlex	Jiménez Becerra	The Effect of Nematic Defects on the Curvature of 3D Cellular Tissues
94	Alice	Perucca	Fibroblast nematicity as a tool to study stromal control on immune migration.
95	Amélie	Godeau	Mechanics of Human Embryo Implantation
96	Anabel-Lise	Le Roux	Acute Cell Stretching Triggers a Rapid Intrinsic Decrease in Plasma Membrane Bilayer Tension
97	Annalisa	Calò	Study of Neuromelanin (NM) accumulation in neurons through AFM micro and nanomechanics
98	Beatriz	Cantero Nieto	Chemically Fueled Lipid Vesicles as Transient Biomimetic Compartments: Insights from Solution-State AFM
99	Carolina	Rodríguez Gallo	Magnetic actuators: Inducing stretching in functional 3D muscle human engineered models.
100	Elena	Faustini	Rational development of a mechanosensitive transcription factor to control gene expression at will
101	Elia	López Serrano	DNA-based phantom cells for local mechanochemical control of intestinal organoid homeostasis
102	Francesca	Mauro	Photo-responsive hydrogels with tunable stiffness for cell mechanobiology
103	Gotthold	Flaeschner	Nuclear geometry predicts local nuclear pore dilation through envelope strain
104	Guillermo	Martínez Ara	An optogenetic toolset to understand and control epithelial mechanical balance.
105	Jorge	Oliver-De La Cruz	Mechanical cues regulate Tau axonal localization through microtubule stabilization
106	Margherita	Gallano	Nuclear Envelope Remodelling upon Mechanical Perturbation
107	Marina	Placci	Redefining Membrane Nanomechanics in Lysosomal Disorders: The Role of GlcCer and Gb3.

N	NAME	SURNAME	TITLE
108	Miguel	González Martín	Design of synthetic mechanosensitive transcription factors
109	Mireia	Valero Puigdomenech	Effects of matrix viscoelasticity on macrophages polarization and their interactions with mesenchymal stem cells
110	Ona	Baguer Colomer	Nuclear mechanics integrate chemical and physical cues to regulate EMT in pancreatic cancer cells
111	Pierre	Ucla	From 2D to 3D: CAF Mechanotransduction in Fibrillar Microenvironments
112	Ricard	Casanovas Zapata	Mechanobiology of Differentiating hiPSC Colonies
113	Rohit	Nautiyal	Nematically guided fracture in brain endothelia
114	Steffen	Grosser	Cell contractility controls epithelial tissues across timescales
115	Vladislav	Petrovskii	Diffusion Anisotropy in Ionically Linked Copolymers
116	Yudish	Varma	Mechanosensing through intermediate filaments alone

N	NAME	SURNAME	TITLE
117	Fleur	Clemenceau	Simultaneous 12-lead ECG for the validation of novel cellulose-based electrodes in human subjects
118	Lluís	Fernández Romero	Curvature Regularized Time Warping for Chromatographic Alignment
119	Mariano	Martín	Systematic mutational mapping reveals optimal amyloid formation for RIPK function
120	Revathi	Ravindran	Towards a Comprehensive Modelling and Design Framework for Predicting Biodegradation at a Macroscale
121	Berta	Tena	Characterization of blood pressure response during rehabilitation in individuals with spinal cord injury and stroke
122	Daniel	Romero Perez	Assessment of Robust Cardiac Beat Detection Methods using Radar-based Physiological Signals
123	Giovanni Vito	Spinelli	hpCSI: an open MATLAB toolbox for preclinical hyperpolarized C13 spectroscopic imaging
124	Inés	Bueso	Development of an Integrated Application for Automatic Data Acquisition and Transmission in Sleep Apnea Monitoring
125	Jaime	Casado García-Consuegra	Spatial tracking of clonal evolution reveals genetic and chemotherapeutic dynamics in Small Cell Lung Cancer
126	Jaume	Rodríguez Soler	Artificial intelligence for the classification of obstructive and central sleep apnea using triaxial accelerometery
127	Mahtab	Mohammadpoor Faskhodi	Assessment of Radar-Based Contactless Respiration Monitoring in Individuals with Stroke and Spinal Cord Injury
128	Renato Eduardo	Yanac Huertas	AnalyCa: a code-free calcium imaging tool, benchmarked in a tauopathy neuronal model
129	Valentina	Schastlivaia	Topology-driven modeling of LRP1-mediated of BBB-crossing nanomedicines: replacing discrete receptor sites counting with surface tension field on homeomorphic manifolds
130	Yolanda	Castillo Escario	Assessment of Night-to-Night Variability in Sleep Apnea using Smartphone-based Sensing and Multimodal Biomarkers

POSTERS

ADDITIONAL POSTERS

N	NAME	SURNAME	TITLE
131	Sustainability	Committee	Building a Culture of Sustainable Science at IBEC: From Green Labs to Institutional Transformation
132	Fátima	Serrano	MicroFabSpace: Enriching Core Facilities to Support IBEC Research

FLASH 1 presented by:

NAME: Mauricio Cano Galván

Mechanotool: An Autonomous Open-Source Software Platform for Large-Scale Multiparametric Analysis of Bio-Atomic Force Microscopy data

Mauricio Cano[1,2], Sophie Strawbridge[1,2], Beatriz Cantero[1,2], Aurora Dols-Pérez[1], Annalisa Calò[1,2], Gabriel Gomila[1,2]

[1] Department of Electronics and Biomedical Engineering, Universitat de Barcelona, Barcelona, Spain

[2] Nanoscale Bioelectrical Characterization, Institute for Bioengineering of Catalonia, Barcelona, Spain

The characterization of biological samples is one of the main applications of Atomic Force Microscopy (AFM) thanks to its ability to perform label-free measurements, under near-physiological conditions, at a nanometric resolution and across multiple physical properties. These include mechanical properties (e.g., Young's modulus, adhesion force) and electrical properties (e.g., dielectric constant) that serve as versatile markers used to identify cell phenotype and differentiation state, nanoparticle structure, composition and integrity, among many other applications. Nevertheless, the current analysis pipelines for multiparametric AFM data can be slow, technically demanding and typically restricted to post-acquisition processing when the sample is no longer accessible for reassessment or parameter adjustment. This results in a large portion of the acquired datasets remaining unused or being discarded, either because the required analysis is too cumbersome or because experimental errors go undetected during imaging. In response to this, we have developed Mechanotool: an open-source, Python-based, modular software platform designed to perform quantitative multiparametric AFM analyses on whole images using both conventional and custom-made analytical models for mechanical and electrical characterization, as well as being able to integrate AI-based characterization algorithms. This pipeline is completely automated, requires no operator intervention after initial parameter configuration, and processes full AFM images in less time than it takes to acquire them, making it ideal for analyzing data in parallel with microscope operation. Moreover, it can be used to post-process entire experimental datasets in batch autonomously. This is achieved by streamlining key manual steps, such as in-image photodiode sensitivity calibration, segmentation of substrate and regions of interest and thresholding for topographical reconstruction using a combination of deterministic and probabilistic techniques. The resulting analysis, obtained with minimal manual intervention, provides users with full parameter maps across multiple physical properties while the sample is still mounted, making full use of all the data acquired and enabling both quality control and insight in real time.

[1] P. Hermanowicz, M. Sarna, K. Burda, and H. Gabryś, "AtomicJ: An open source software for analysis of force curves," Review of Scientific Instruments, vol. 85, no. 6, p. 063703, Jun. 2014, doi: 10.1063/1.4881683.

FLASH PRESENTATION | ADVANCED MICROSCOPY

FLASH 2 presented by:

NAME: Zahra Saeidikia

Imaging and modelling PEG-PLA nanoparticles and their disassembly of Aβ42 fibrils

Zahra Saeidikia[1,2,3], Jose Muñoz-López[1,4], Nisha Pawar Chawhan[1], Giuseppe Battaglia[1,5], and Lorena Ruiz-Pérez[1,3,6]

[1] *Institute for Bioengineering of Catalunya, IBEC, Barcelona, Spain*
[2] *Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain*
[3] *Department of Applied Physics, Faculty of Physics, University of Barcelona, Barcelona, Spain*
[4] *Faculty of Chemistry, University of Barcelona, Barcelona, Spain*
[5] *Catalan Institution for Research and Advanced Studies, ICREA, Barcelona, Spain*
[6] *Serra Húnter Fellow, Barcelona, Spain*

Dementia affected 57.4 million people worldwide in 2019 and is forecast to reach 152.8 million by 2050 [1]. Amyloid beta 42 is the most aggregation-prone of the amyloid beta variants, with its two additional hydrophobic C-terminal residues driving nucleation and elongation into insoluble, beta-sheet-rich fibrils that accumulate as parenchymal plaques [2]. FDA-approved antibodies such as Lecanemab do engage aggregated species, notably protofibrils, yet their action proceeds largely through clearance rather than direct disassembly of the fibril [3]. Multivalent assemblies built from block copolymers offer an alternative, since ligand number and steric control can be tuned towards epitopes exposed only after assembly [4]. Establishing whether such particles remodel mature fibrils calls for a method that reaches these structures while hydrated. Liquid Phase Transmission Electron Microscopy (LPTEM) emerges as a powerful tool, combining high spatial and temporal resolution with access to the dynamics of soft matter in its native state [5], and Coarse-Grained Molecular Dynamics simulations complement it at the molecular scale.

Here we characterise peptide-functionalised amphiphilic PEG-PLA nanoparticles, selected from a large library by thioflavin T aggregation kinetics, and their action on preformed Aβ42 fibrils. LPTEM resolution allowed us to separate the hydrophobic core and hydrated corona within single polymeric nanoparticles in solution, while the simulations report ligand density, chain packing, and the particle's radial organisation. Sampling the mixtures every 30 minutes over five hours, we observed the fibrils breaking into progressively shorter fragments that remained insoluble, and confirmed the same behaviour in LPTEM.

Combining LPTEM with coarse-grained simulations offers a route to visually screen the physical and molecular mechanisms of newly developed drugs targeting Aβ aggregation. The formulation shown here is a demonstration, and the same approach transfers to other formulations and other misfolded proteins.

References

1. GBD 2019 Dementia Forecasting Collaborators. Lancet Public Health. 2022;7:e105. 2. Cohen SIA, et al. Proc Natl Acad Sci USA. 2013;110:9758.

3. van Dyck CH, et al. N Engl J Med. 2023;388:9.

4. Muñoz-López J, et al. J Am Chem Soc. 2026;148:4839.

5. Leite DM, et al. Brain Commun. 2022;4:fcac039.

FLASH 3 presented by:

NAME: Esteban Suárez Baquero

Development of an All-Optical Platform for Imaging and Holographic Manipulation of Neural Circuits in Behaving Mice

Esteban Suárez Baquero[1], Courtney Hospes[1], Nicolò Accanto[1]

[1] Nonlinear Photonics for Neuroscience, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain.

In our group, we develop advanced microscopy systems to study neuronal circuits and their interaction with animal behavior. Understanding how neural ensembles orchestrate complex behaviors requires tools that can record and manipulate brain activity with high spatiotemporal resolution.

Since the group started at IBEC, we have built a comprehensive, all-optical platform capable of addressing these challenges across different experimental scales. We have developed a versatile two-photon microscope that can study large neuronal circuits in the mouse cortex and, with specialized adaptations like our flexible fiberscope, investigate smaller targeted circuits in freely moving animals performing natural behaviors. This platform is driven by two main technological pillars: high-speed two-photon microscopy for the rapid imaging of neuronal calcium dynamics, and precise holographic photostimulation for the targeted manipulation of selected neurons.

In this talk, I will describe the technological milestones and results we have obtained in the IBEC laboratory with these novel optical architectures. I will showcase how our system achieves cellular precision to monitor and control neural activity in vivo.

Furthermore, I will introduce our future research direction: leveraging these state-of-the-art methods to uncover the neural basis of memory. We are expanding our technology into a dual-region approach to simultaneously image and photostimulate interconnected networks, specifically the dialogue between the hippocampus and the prefrontal cortex. This causal, inter-regional access will be crucial for understanding how memories are consolidated and why they pathologically persist in trauma related conditions such as PTSD.

POSTER | ADVANCED MICROSCOPY

POSTER 4 presented by:

NAME: Belle Clayton

Uncovering the Transcriptional Regulation of Ribonucleotide Reductases in *Pseudomonas aeruginosa*

Belle Clayton[1,2], Ángela Martínez[1,2,], Eduard Torrents[1,2,*]*

[1] Bacterial infections and antimicrobial therapies group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST). Baldiri Reixac 15-21. 08028 Barcelona, Spain.

[2] Microbiology Section, Department of Genetics, Microbiology and Statistics, Faculty of Biology, University of Barcelona, 643 Diagonal Ave., 08028, Barcelona, Spain.

Ribonucleotide reductases (RNRs), encoded by *nrd* genes, are a family of enzymes that catalyze the conversion of ribonucleotides into the deoxyribonucleotides required for DNA synthesis and repair. RNRs provide the only pathway for the *de novo* production of these essential building blocks, making their activity critical for cellular survival. RNRs are divided into three different classes (I, II, and III) depending on their utilization of metal cofactors and their reaction with oxygen. *Pseudomonas aeruginosa* is an opportunistic pathogen associated with chronic infections and is one of the few organisms known to encode all three classes of RNRs, allowing it to maintain DNA synthesis under a wide range of environmental conditions. This flexibility is particularly important during infection, where the bacterium can encounter large fluctuations in oxygen, nutrient, and metal availability. RNR expression therefore needs to be tightly coordinated in response to these changing conditions. Although some regulators of the *nrd* genes have already been identified, the broader network controlling their expression remains poorly understood.

This work combines molecular biology, microbiology, and biochemical approaches to investigate the role of transcription factors in *nrd* regulation. A better understanding of how *P. aeruginosa* coordinates RNR expression could provide further insight into how this pathogen adapts DNA synthesis and growth in response to its environment, while potentially uncovering new targets for antimicrobial intervention.

This study was supported by grants 101168976 – SPM4.0 from the European Commission “Horizon Europe (HORIZON)- HORIZON TMA MSCA Doctoral Networks”; PID2024-158933OB-I00 funded by MCIN/AEI/10.13039/501100011033 and “ERDF A way of making Europe”; the CERCA program and AGAUR-Generalitat de Catalunya (2021SGR01545), by the European Regional Development Fund (FEDER). E.T. is a researcher of the ICREA Academia 2025 program. BC is thankful to the Horizon Europe (European Commission) for its financial support through a Horizon TMA MSCA Doctoral Networks SPM 4.0.

POSTER 5 presented by:

NAME: Courtney Christine Hospes

2-Photon Imaging and Manipulation of Memory Circuits in Freely Moving Mice

Courtney Hospes[1], David Esteban Suarez Baquero[1], Nicoló Accanto[1]

[1] Nonlinear Photonics for Neuroscience Group, Institute for Bioengineering of Catalonia (IBEC), Parc Cientific Barcelona, Barcelona, Spain

Imagine if the process of memory storage in the brain could be understood at a deep enough level to create artificial memories or even erase traumatic ones altogether. To understand memory consolidation, or how the brain processes recent memories in the hippocampus and stores them as long-term memories in the prefrontal cortex, neuroscientists study the engram, the physical trace of a memory, cell by cell. We study engrams in mice by taking advantage of calcium imaging during a behavioral task. We optically access the brain through a cranial window, the surgical preparation that allows us to visualize the brain while it is active. Using an all-optical imaging system designed for freely moving animals in the 2-photon regime, we monitor hundreds of neurons across different brain regions at once with single-cell resolution. This imaging system is coupled to a multicore fiber inserted through the optical implant, enabling photostimulation with single-cell targeting. We use a fast-acting, sensitive fluorescent calcium sensor, GCaMP7f, and a high-performing opsin, ChRmine, for cellular precision and temporal resolution. Once we have identified the target engram, we interrogate it through photostimulation, turning specific neurons on and off optogenetically to test for causality. The animal's physical response to photostimulation indicates whether it is reliving the experience: if the mouse reacts similarly to the behavioral task when we reactivate the engram, we can demonstrate that the physical trace of the memory is the link between a cluster of cells and a lived experience. Once we map the neural circuits of memories, we can investigate how to intervene when these circuits become pathological, as in Alzheimer's or PTSD.

POSTER | ADVANCED MICROSCOPY

POSTER 6 presented by:

NAME: Gonzalo Alonso Reillo

Metabolic Analysis in real time by using benchtop NMR Technology

Gonzalo Alonso Reillo, Giovanni Vito Spinelli, Irene Marco-Rius

Institute of Bioengineering of Catalonia, Barcelona, Spain.

Real-time metabolism is a field of study that has grown considerably in the context of precision medicine. For its investigation, Nuclear Magnetic Resonance (NMR) and Magnetic Resonance Imaging (MRI) have become the primary non-invasive and quantitative tools. These techniques can detect cancer-induced metabolic reprogramming through ^{13}C Magnetic Resonance (^{13}C MR) combined with dissolution Dynamic Nuclear Polarization (dDNP). ^{13}C MR enables the study of specific metabolic pathways, while dDNP enhances the signal by more than 10^5-fold [1]. This approach has been demonstrated both *in vitro* and *in vivo* [1].

In vitro experiments have been performed using Organ-on-a-Chip (OoC) devices with MRI and high-field NMR spectrometers. However, our laboratory previously developed the first commercially available 1.4 T benchtop NMR platform compatible with OoC devices for real-time metabolic studies. This unique spectrometer uses a permanent low-field magnet instead of a superconducting one, making it affordable and easy to maintain. It has also been shown to provide robust and reproducible results [2].

Nevertheless, low-field spectroscopy reduces both spectral resolution and the signal-to-noise ratio (SNR). To overcome this limitation, we are developing a spatial-spectral pulse sequence that enables the selective detection of specific metabolites.

This pulse sequence reduces noise and spectral artifacts, while its combination with dDNP further increases the SNR [3]. This approach allows the simultaneous detection of different metabolic pathways within a single acquisition. By selectively enhancing metabolites like Pyruvate or DHAc as substrates, and exciting them and their products, such as Lactate or Glycerol, we can extract more metabolic information from a single experiment [4]. We are performing simulations that will be validated using well-known samples. We expect to quantify these metabolites during *in vitro* experiments while suppressing signals from less relevant compounds, enabling the generation of a more comprehensive metabolic profile.

[1] Marco-Rius I, et al. *Magma (New York, N.Y.). 2021; 34(1), 49–56.*

[2] Azagra M, et al. *Anal. Chem. 2026; 98 (4): 2701–2708.*

[3] Lau, A.Z, et al. *NMR Biomed 2011; 24: 988-996.*

[4] Marco-Rius I, et al. *Magn. Reson. Med. 2017; 77: 1419-1428.*

POSTER 7 presented by:

NAME: Jhon Pazos

Enhanced Scanning Dielectric Microscopy: On-Resonance operation for improved signal-to-noise ratio in nanoscale dielectric characterization

Jhon Pazos[1,2], Gabriel Gomila[1,3]

[1] Institute for Bioengineering of Catalonia (IBEC), Nanoscale Bioelectrical Characterization Group, Barcelona, Spain
[2] Physics Faculty, University of Barcelona, Barcelona, Spain
[3] Department of Electronics and Biomedical Engineering, University of Barcelona, Barcelona, Spain

The dielectric properties of biological materials govern their response to electric fields and influence molecular electrostatic interactions and cellular bioelectric processes. Their quantitative mapping at the nanoscale offers label-free insight into local dielectric heterogeneity that is inaccessible to bulk measurements. Scanning Dielectric Microscopy (SDM) has enabled dielectric characterization of nanoparticles, viruses, bacterial and eukaryotic cells, and DNA packaged within bacteriophages. However, its limited signal-to-noise ratio (SNR) has hindered measurements of weakly polarizable molecular-scale systems.

In conventional force-sensing SDM, an alternating voltage applied to a conductive atomic force microscopy probe produces an electrostatic force at twice the electrical excitation frequency. The corresponding cantilever oscillation is measured along tip– sample approach curves and converted into the capacitance gradient, dC/dz, for dielectric quantification. Off-resonance operation simplifies this conversion but generates small oscillation amplitudes. Improving sensitivity by using softer cantilevers or higher voltages is constrained by premature jump-to-contact.

Here, we develop and experimentally validate an on-resonance SDM methodology in which the second-harmonic electrostatic force drives the cantilever at its mechanical resonance frequency, amplifying the response approximately by its quality factor, Q. A hydrodynamic model incorporating air-squeezing effects predicts that the resonance frequency changes only slightly during approach, whereas Q decreases significantly near the surface. We determine this distance-dependent Q experimentally from oscillation-amplitude spectra and account for it when recovering quantitative capacitance-gradient curves. Nonlinear effects associated with large oscillation amplitudes are also assessed to establish suitable measurement conditions. The resulting model predicts an SNR improvement exceeding one order of magnitude compared with optimized off-resonance SDM under practical conditions.

We validate the method on patterned SiO_2 pillars supported by highly doped silicon, obtaining a relative dielectric constant of approximately 4.2, consistent with the expected value for SiO_2. Fits to the experimental capacitance-gradient curves yield a residual standard deviation of approximately 0.4 zF/nm. These results establish on-resonance SDM as a promising approach for sensitive, quantitative nanoscale dielectric measurements and provide a foundation for future investigations of nanofibrils, DNA, proteins, and other molecular-scale systems.

POSTER | ADVANCED MICROSCOPY

POSTER 8 presented by:

NAME: Raquel García Olivas

Microscopy Characterization Facility: Enabling Advanced and Quantitative Imaging

Alejandro Escobar[1] and Raquel García[1]

Microscopy Characterization Facility – Core Facilities Unit - Institute for Bioengineering of Catalonia, Barcelona, Spain

The Microscopy Characterization Facility at IBEC provides researchers with access to advanced optical microscopy technologies for a wide range of biomedical and bioengineering applications. In addition to state-of-the-art instrumentation, the facility offers training, experimental design support, and expert guidance to both internal and external users, facilitating the implementation of advanced imaging workflows and the generation of high-quality, reproducible data.

The facility currently includes several imaging systems: the confocal LSM800, widefield microscopes (LSM700 and Axio Observer 7), a STORM super-resolution microscope, and an advanced workstation for image analysis. Together, these platforms enable imaging and quantitative analysis across multiple spatial scales, from single molecules to living cells.

The facility is also expanding its capabilities with the upcoming incorporation of a Brillouin microscope (co-managed with Manuel Salmeron's group) and a new multiphoton confocal microscope. These additions will broaden the range of available applications and enable new approaches for functional and biomechanical imaging.

This poster also presents guidelines for the appropriate reporting of microscopy methods and results in publications using data acquired at the microscopes in IBEC. In addition, recommendations for properly acknowledging the facility are provided to ensure appropriate recognition of its contribution and to support future equipment acquisition and continued development of the facility.

Overall, the Microscopy Characterization Facility aims to provide an integrated imaging platform combining advanced microscopy technologies, quantitative image and expert support to enable precise and quantitative approaches in biomedical and bioengineering research.

POSTER 9 presented by:
NAME: Sepideh Sadat Mirhosseini

Development of a Two-Photon Holographic Mesoscope for Large-Scale Optogenetic Stimulation with Single-Cell Resolution

Sepideh Sadat Mirhosseini[1], Nicolò Accanto[1]

[1] Nonlinear Photonics for Neuroscience Group, Institute for Bioengineering of Catalonia(IBEC), 08028, Barcelona, Spain

Understanding how neuronal circuits generate perception, cognition, and behavior requires technologies capable of monitoring and manipulating large neuronal populations with high spatial precision. The combination of two-photon (2P) microscopy, genetically encoded activity indicators, and optogenetic actuators has enabled all-optical interrogation of neural circuits in vivo with single-cell resolution. However, current 2P optogenetic approaches are largely restricted to local neural networks spanning less than 1 mm due to limitations in photostimulation field of view (FOV).

Recent advances in 2P mesoscopy have expanded imaging FOVs to several millimeters while preserving cellular resolution. Nevertheless, the photostimulation area achievable with holographic techniques remains limited to approximately 1 × 1 mm^2. This limitation originates from the finite pixel count of commercially available spatial light modulators (SLMs) and the optical constraints required to maintain micrometer-scale focusing at the sample plane. Consequently, current systems cannot fully exploit the large imaging capabilities of mesoscopes for large-scale optogenetic manipulation. The objective of this project is to develop the first **Two-Photon Holographic Mesoscope** capable of delivering precise optogenetic stimulation across a **5 × 5 mm^2 field of view** while maintaining single-cell spatial resolution.

POSTER | ADVANCED MICROSCOPY

POSTER 10 presented by:

NAME: Tom White

Pathogenic collagen VI variants impair extracellular matrix mechanics at the nanoscale

Tom White[1,2], Stefano Chiodini[2], Arístides López-Marquez[3], Carmen Badosa[3], Cecilia Jiminez-Mallebrera[3], Josep Samitier[1], Anna Lagunas[1], Marina Giannotti[2]

[1] IBEC, Nanobioengineering Group, Barcelona, Spain
[2] IBEC, Nanoprobes and Nanoswitches Group, Barcelona, Spain
[3] Laboratorio de Investigacion Aplicada en Enfermedades Neuromusculares, Institut de Recerca Sant Joan de Deu, Barcelona, Spain

Collagen VI forms a distinct microfibrillar network in the extracellular matrix (ECM), interacting with a range of structural matrix proteins to organise tissue architecture. Mutations to any of the three major genes which encode collagen VI leads to a group of neuromuscular disorders known as Collagen type VI-related congenital muscular dystrophies (COL6-Rds). In this study, through atomic force microscopy-force spectroscopy, we assess how inclusion of these mutant microfibrils impact the nanomechanical properties of decellularised matrices produced from primary dermal fibroblasts. By correlating these results with the organisation of specific ECM proteins, we further demonstrate how structural changes can drive altered cellular behaviour.

Whilst no effective treatment is currently available for COL6-RDs, novel genetic therapies have emerged as a strategy to target different classes of mutation responsible for this disease. Hence, developing new tools to assess the efficacy of these treatments has become imperative for their clinical translation. We report that genetic editing of patient cells can successfully restore the elastic modulus of the ECM to control levels. These findings suggest that nanomechanical analysis provides a functional readout for evaluating cellular response to gene therapies, serving as a valuable tool for future clinical applications.

POSTER 11 presented by:

NAME: Yoel Melul Steinfeld

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

Yoel Melul Steinfeld[1], David Esteban Suárez Baquero[1], Courtney Christine Hospes[1], Sepideh Sadat Mirhosseini[1], Nicolò Accanto[1]

[1] Institute of Bioengineering for Catalonia (IBEC), Barcelona, Spain

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.

FLASH PRESENTATION | ADVANCED THERAPEUTIC SYSTEMS

FLASH 12 presented by:

NAME: Claudia Camarero-Hoyos

A multifaceted approach to define a novel family of antimalarial compounds: the role of protein aggregation in *Plasmodium*

Claudia Camarero-Hoyos[1,2,3], Ana Mallo-Abreu[4,5], Antonino Nicolò Fallica[1,2], Samuel Pazicky[6], Zbynek Bozdech[6], Ghizal Siddiqui[7], Darren J. Creek[7], Diego Muñoz-Torrero[4,5], Yunuen Avalos-Padilla[1,2], Xavier Fernàndez-Busquets[1,2,8]

[1] *Barcelona Institute for Global Health (ISGlobal), Barcelona, Spain.*
[2] *Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain.*
[3] *Doctoral School of Biotechnology, Faculty of Pharmacy and Food Sciences, University of Barcelona, Barcelona, Spain.*
[4] *Laboratory of Medicinal Chemistry, Faculty of Pharmacy and Food Sciences, University of Barcelona, Barcelona, Spain.*
[5] *Institute of Biomedicine (IBUB), University of Barcelona, Barcelona, Spain.*
[6] *School of Biological Sciences, Nanyang Technological University, Singapore, Singapore.*
[7] *Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Australia*
[8] *Nanoscience and Nanotechnology Institute (IN2UB), University of Barcelona, Barcelona, Spain.*

With frontline drug resistance stalling progress against malaria (282 million cases and 610,000 deaths in 2024), new therapeutic strategies must exploit uncharacterised biological vulnerabilities in *Plasmodium*. One such target is protein aggregation, an essential process across the parasite's life cycle that remains poorly understood. A family of promising candidates is YAT#, derived from YAT2150, a bis(styrylpyridinium) salt with potent antiplasmodial activity that has been shown to reduce protein aggregation in live parasites. Given that *in vitro* resistance has not been detected for YAT# , a set of several complementary approaches is currently being employed to better define the mechanism of action of these compounds. A combination of proteomic analyses including pull-down assays, Cellular Thermal Shift Assays (CETSA) and Solvent Shift Assays, alongside transcriptomic profiling, is being applied to map their molecular targets and immediate downstream responses. Preliminary data show dysregulation across multiple target proteins with distinct profiles for each of the compounds tested, pointing to a broad mechanism that disrupts dynamic protein-interaction networks. Ultimately, this multifaceted framework aims to better understand YAT#'s disruption of parasite function, thereby defining the essential role of protein aggregation in *Plasmodium* to guide new approaches to malaria treatment.

Funding: The project that gave rise to these results has received funding from “la Caixa” Foundation under the grant agreement LCF/PR/HR24/52440003.

FLASH 13 presented by:

NAME: Dario Castellana

Dual-Action 3D Biomaterial for Radiotherapy: Protection and Regeneration of Tissue during X-ray Treatment

Dario Castellana[1,2,4], Nuno M Coehlo[1], Oscar Castaño[1,3], Elisabeth Engel[1,2,4]

[1] Biomaterials for regenerative group, IBEC, Barcelona, Spain
[2] Ciber en Bioingenieria, Biomateriales y Nanomedicina, Ciber-BBN, Madrid, Spain
[3] Department of Electronics and Biomedical Engineering, facuty of physics, Universitat de Barcelona, Barcelona, Spain
[4] IMEM-BRT group, Department of Material science, Universitat Politecnica de Catalunya, Barcelona, Spain

Radiotherapy for cancer patients remains limited by the side effects of ionizing radiation on healthy tissues. Amifostine is the only FDA-approved ROS-scavenger radioprotective drug for Head and Neck Squamous Cell Carcinoma, but its clinical utility is limited by suboptimal therapeutic effects under standard systemic delivery.

To optimize local drug concentration and enhance amifostine's retention in the X-ray-irradiated area, we propose the application of a local delivery system intended to improve and extend the therapeutic window of the drug. We hypothesized that a GelMA-based system incorporating amifostine-loaded PLGA nanoparticles and calcium/zinc ionic nanoparticles could simultaneously radioprotect irradiated tissue and support regeneration of resected areas.

Amifostine was encapsulated in spherical PLGA nanoparticles (~250 nm) using a double-emulsion synthesis protocol. This approach achieved >90% efficiency before embedding the nanoparticles in the GelMA hydrogel precursor solution, enabling controlled and tunable drug release kinetics.

To trigger and support the regeneration of new tissue, a bottom-up protocol was developed to synthesize calcium- and zinc-based ionic nanoparticles (iNPs). These iNPs were incorporated into aligned PLGA fibers within an electrospun fiber mat.

The final delivery system was assembled by depositing the iNP-loaded PLGA fiber mat onto the GelMA hydrogel precursor solution containing amifostine-loaded PLGA NPs, followed by UV crosslinking to stabilize the composite structure.

The composite biomaterial delivers a dual therapeutic effect: rapid amifostine release reduces ROS concentration in the irradiated area during the critical early phase, while the sustained release of bioactive ions from the fiber mat supports tissue regeneration and vascularization over time.

FLASH PRESENTATION | ADVANCED THERAPEUTIC SYSTEMS

FLASH 14 presented by:

NAME: Esra Kasapgil

Endothelium-mimicking hemocompatible coatings for artificial placenta systems

*Esra Kasapgil[1,2], Jenny Englert[1,3], Lena Witzdam[1,3], Elisenda Eixarch Roca[4], Josep Samitier-Marti[1], Eduard Gratacos[4], Cesar Rodriguez Emmenegger[1,3,5]**

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain
[2] Izmir Bakircay University, Izmir, Türkiye
[3] DWI – Leibniz Institute for Interactive Materials e.V., Aachen, Germany
[4] BCNatal Fetal Medicine Research Center (Hospital Clínic and Hospital Sant Joan de Déu), Universitat de Barcelona, Barcelona, Spain
[5] Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain

Preterm birth is the leading cause of death in children under five, accounting for over one million deaths each year. To support these vulnerable infants, continuous oxygenation similar to what they receive in the womb is essential. However, no extracorporeal oxygenator currently exists that can safely meet this need. The main challenge is poor hemocompatibility, which leads to clotting and device failure. We developed a bioinspired coating that mimics the natural endothelium by combining three key functions: stealth, modulation, and interaction. This multifunctional coating reduces the need for systemic anticoagulants and helps prevent thrombosis. It is composed of antifouling brush-like polymer coatings, molecules that regulate coagulation, and fibrinolytic system. Together, they recreate the natural ability of the endothelium to repel proteins, control coagulation, and support clot breakdown. The coating maintained its antifouling properties even after the enzymes were immobilized. These enzymes remained active and were able to capture activated coagulation factors such as FXIIa, FXa, and kallikrein directly on the surface. Impressively, the coating digested a macroscopic clot within 3.5 hours. We tested this design in mini oxygenator models and observed a significant reduction in clot formation on coated fibers without compromising oxygenation performance. This work offers a breakthrough solution for hemocompatible artificial placenta systems and has the potential to greatly improve outcomes for premature infants.

FLASH 15 presented by:

NAME: Joaquín Martínez Tambella

Restoration of edge detection and visually guided behavior in ambient white light with photoswitchable small molecules

Joaquín Martínez-Tambella,[1,2,3], Rosalba Sortino,[1,2,3], Aleix González-Díez,[4] Santiago Milla-Navarro,[5,6] Víctor Paleo-García,[5,6], Ekin Opar,[1,2,3], Fabio Riefolo,[1,2,3] Carlo Matera,[1,3]Jordi Hernando,[7] Alexandre M. J. Gomila,[1,2,3], Núria Camarero,[1,3] Carme Serra,[4] Xavier Gómez-Santacana,[4] Amadeu Llebaria,[4,8] Xavier Rovira,[4] Pedro de la Villa[5,6], Pau Gorostiza[1,3,9]

[1] *Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain*
[2] *University of Barcelona Doctorate Program, Barcelona, Spain*
[3] *CIBER-BBN, Madrid, Spain*
[4] *Medicinal Chemistry and Synthesis (MCS) Laboratory, Institute for Advanced Chemistry of Catalonia (IQAC-CSIC), Barcelona, Spain*
[5] *University of Alcalá de Henares (UAH), Alcalá de Henares, Spain*
[6] *Institute Ramón y Cajal of Health Research (IRYCIS), Madrid, Spain*
[7] *Autonomous University of Barcelona (UAB), Cerdanyola del Vallès, Spain*
[8] *Synthesis of High Added Value Molecules (SIMChem), Institut de Química Avançada de Catalunya (IQAC-CSIC), Barcelona, Spain*
[9] *Catalan Institution of Research and Advanced Studies (ICREA), Barcelona, Spain*

Blinding diseases due to degeneration of photoreceptors (PhRs) like geographic atrophy (GA) and retinitis pigmentosa (RP) leave the rest of the retinal circuitry largely intact, albeit unable to respond to light. Photopharmacology can develop photoswitchable small molecules to restore vision impairment by conferring light sensitivity to ion channels that are widely expressed in the remaining inner retinal neurons, and a first-in-human clinical trial is ongoing. Here, we have developed novel photoswitchable small molecule ligands of mGlu6 receptors, which are located exclusively at the dendrites of ON bipolar cells (postsynaptic to PhRs) and can leverage a privileged position to mimic physiological signals in the remnant retinal circuit. These photoswitchable ligands (prosthe6) thus act as 'molecular prostheses' that can restore the light input to the retina via upstream-targeted control of the circuit after PhRs degeneration. Prosthe6 compounds are allosteric, drug-like, water soluble, and display outstanding in vitro properties including full efficacy, nanomolar potency, fast deactivation in ambient white light, and fast reactivation in the dark. These drugs readily recover the edge detection ability of blinded zebrafish larvae and restore the innate light avoidance behavior in mouse models of blindness (GA and RP). These effects are mediated by mGlu6 receptors in vivo. In addition, at least two compounds (prosthe6-12 and -15) can restore sight by topical administration and display promising safety properties to become potential drug candidates for sight restoration in patients of degenerative blinding diseases.

FLASH PRESENTATION | ADVANCED THERAPEUTIC SYSTEMS

FLASH 16 presented by:

NAME: Carlos Moreno Yruela

Nucleosome-Based Platforms to Decipher Histone Deacetylase Mechanisms and Develop Modulators in High Throughput

C. Moreno-Yruela,[1,2] P. N. Foteva,[2] E. Calvino-Sanles,[2] B. E. Ekundayo,[3] D. Ni,[3] T. N. Hansen,[4] L. K. Petersen,[4] L. K. Larsen,[4] A. Taranta,[4] N. J. V. Hansen,[4] H. Stahlberg[3] & B. Fierz[2]

[1] Enzyme Sensors and Chemical Probes group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Barcelona, Spain

[2] Laboratory of Biophysical Chemistry of Macromolecules (LCBM), Institute of Chemical Sciences and Engineering (ISIC), School of Basic Sciences, EPFL, Lausanne, Switzerland

[3] Laboratory of Biological Electron Microscopy (LBEB), Institute of Physics (IPHYS), School of Basic Sciences, EPFL, Lausanne, Switzerland

[4] Vipergen ApS, Copenhagen, Denmark

The sirtuin enzymes SIRT6 and SIRT7 are histone deacetylases regarded as therapeutic targets in pancreatic cancer and hepatocellular carcinoma. However, inhibitor screening has proved challenging thus far, as current screening solutions are based on small fluorogenic peptide substrates, while SIRT6 and SIRT7 are only active on endogenous substrate assemblies with nucleic acids such as the nucleosome, *i.e.*, 147 bp of DNA wrapped around a histone octamer. Here, we take advantage of the intrinsic nucleosome recognition mechanisms of SIRT6 and SIRT7 to develop a robust nucleosome-based platform for inhibitor screening and detailed mechanistic studies. We produced semi-synthetic nucleosomes with functional groups for (1) mechanism-based crosslinking and (2) activity detection. The first strategy served to stabilize the complex of SIRT7 with its preferred nucleosome substrates and determine the mechanisms of activation and selectivity via high-resolution cryo-EM structures. We found that SIRT7 docks onto nucleosomes through its helical N-terminal domain and positions the catalytic pocket in close proximity to lysine K36 of histone H3. These structural insights enabled the second strategy, where we installed an acyl-lysine quencher next to a non-disruptive fluorophore, so that sirtuin-mediated quencher cleavage provides a fluorescence signal in real time. These fluorescent nucleosomes are the most efficient substrates reported to date, permitted inhibitor screening with Z' values over 0.8, and afforded a potent and selective SIRT6 inhibitor active against cancer cell migration. In conclusion, we present a solution for advanced enzyme characterization and screening, which paves the way for drug development against enzyme targets currently inaccessible.

POSTER 17 presented by:

NAME: Adriano Caliari

Engineering superselectivity in a synthetic endocytosis model

Adriano Caliari[1], Giuseppe Battaglia[1]

[1] Institute for Bioengineering of Catalunya, Barcelona, Spain

Understanding cargo uptake via endocytosis is fundamental to deciphering cellular functions, diseases, and engineering next-generation therapeutics. While several molecular actors in this process have been identified, living cells are complex systems that make it difficult to trace behavior back to first principles. Bottom-up synthetic biology offers a solution: constructing systems of known composition that replicate cellular processes and reveal gaps in current models.

This project investigates the biophysical underpinnings of endocytosis in a minimally complex system to elucidate the role of superselectivity in cargo internalization. Giant unilamellar vesicles (GUVs) serve as cell membrane models, decorated with synthetic receptors composed of short DNA sequences. Complementary ligand strands attached to model colloidal particles mediate cargo association with these synthetic cells. By carefully designing ligand and receptor sequences, we can precisely control binding energy and observe consequent membrane deformation, identifying the physical requirements for cargo binding and internalization in a fully defined synthetic system.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 18 presented by:

NAME: Ainhoa González Caelles

Photomechanical Vapor Nanobubble Engineering of Whole-Cell Vaccines for Bladder Cancer Prophylaxis

Ainhoa G. Caelles[1,3,4,†], Núria Sabando García[2,†], Noemí Traba[2], Joan Pagès[5], Cecilia Cabrera[5], Ana Garcia Hidalgo[1], Jana Ramon[6], Deep Punj[6], Kevin Braeckmans[6], Annabel F. Valledor[7,8], Gertruda Chomiciute[9], Ibane Abasolo[9,10], Samuel Sánchez[1,11,], Esther Julián Gomez[2,*], Juan C. Fraire[1,9,10,*]*

[1] *Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Baldiri i Reixac 10-12, 08028 Barcelona, Spain.*
[2] *Genetics and Microbiology Department, Faculty of Biosciences, Autonomous University of Barcelona, Barcelona, Spain.*
[3] *Nanobots Therapeutics S.L., Carrer Baldiri i Reixac, 4, 08028 Barcelona, Spain.*
[4] *Department of Biochemistry and Physiology, Faculty of Pharmacy and Food Sciences, University of Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain.*
[5] *IrsiCaixa AIDS Research Institute, Hospital Germans Trias i Pujol, Carretera de Canyet s/n, 08916 Badalona, Barcelona, Spain.*
[6] *Laboratory for General Biochemistry and Physical Pharmacy, Faculty of Pharmaceutical Sciences, Ghent University, 9000 Ghent, Belgium.*
[7] *Department of Cell Biology, Physiology and Immunology, Faculty of Biology, University of Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain.*
[8] *Institute of Biomedicine of the University of Barcelona (IBUB), Av. Diagonal 643, 08028 Barcelona, Spain.*
[9] *Institute for Advanced Chemistry of Catalonia (IQAC-CSIC), Jordi Girona 20, 08034 Barcelona, Spain.*
[10] *Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Instituto de Salud Carlos III, Barcelona, Spain.*
[11] *Catalan Institute for Research and Advanced Studies (ICREA), Passeig de Lluís Companys 23, 08010 Barcelona, Spain.*
[†] *These authors contributed equally.*

Whole-cell cancer vaccines promise broad antigen presentation, yet traditional inactivation methods often damage crucial danger signals needed to prime robust immunity. Here, we demonstrate a drug-free, photomechanical strategy to engineer whole-cell bladder cancer vaccines using laser-induced vapor nanobubbles (VNB) driven by dextran-coated iron oxide nanoparticles. Brief pulsed-laser irradiation of MB49 urothelial carcinoma cells triggered rapid immunogenic cell death (ICD), characterized by elevated ATP/HMGB1 release and superior surface calreticulin exposure compared to chemotherapy (doxorubicin). In prophylactic mouse models, VNB-engineered vaccines completely prevented MRI-detectable orthotopic tumor formation and markedly reduced subcutaneous engraftment. Moreover, VNB vaccination reshaped the tumor microenvironment by expanding effector/memory lymphoid populations and driving a significant $CD8^+$ T-cell infiltration (7% of $CD45^+$ cells)— outperforming doxorubicin controls. This work establishes laser-induced VNBs as a controllable tool for custom whole-cell vaccine fabrication, offering a promising drug-free strategy to enhance tumor prophylaxis.

POSTER 19 presented by:

NAME: Albert Ripoll

Novel Alginate Lyases Enhance Antibiotic Efficacy Through Biofilm Matrix Disruption in *Pseudomonas aeruginosa*

Albert Ripoll[1,2], Núria Blanco-Cabra[1,2], Eduard Torrents[1,2]

[1] Bacterial Infections: Antimicrobial Therapies, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology, Barcelona, Spain.

[2] Microbiology Section, Department of Genetics, Microbiology and Statistics

Bacterial biofilms are groups of individual cells embedded in a self-produced extracellular matrix (ECM) composed of polysaccharides, extracellular DNA (eDNA), proteins, lipids, and water. Biofilms can be found attached to a surface or as free-floating cell aggregates. The ECM plays a major role in the biofilm architecture since it constitutes its scaffold and, very importantly, serves as a biochemical barrier that protects bacterial cells from the environment, the host immune system, and antibiotics. Therefore, the ECM has emerged as a potential therapeutic target to combat biofilm infections, and most strategies focus on degrading its different components by enzyme degradation. The efficacy of these kinds of approaches depends on the biofilm composition and the bacterial species that form it. Noteworthily, biofilm-dispersing enzymes always need to be accompanied by antibiotic treatment since they do not possess antibiotic activity per se.

In this work, we explore the potential antibiofilm activity of two newly synthesized poly M/G alginate lyases belonging to the PL7 family, AlgilyBIAT1 and AlgilyBIAT2, on mature biofilms of *Pseudomonas aeruginosa* PAO1 wt and an overproducing alginate strain (PAO1 Δ*mucA*). Our approach is based on the potential capacity of our enzymes to selectively degrade alginate, a polyanionic polysaccharide present in mature *P. aeruginosa* biofilms that plays a key role in maintaining the ECM. Based on sequence alignments with other well-described alginate lyases and AlphaFold 3 structural predictions, we identified their putative active and alginate-binding sites. We have also optimized their purification strategy and assessed their activity in sodium alginate, planktonic cultures, static biofilms, and dynamic biofilms. Moreover, we have studied their efficacy in degrading the biofilm's ECM polysaccharides by confocal microscopy. Preliminary results indicate that AlgilyBIAT1 presents a promising antibiofilm activity and enhances antibiotic efficacy in both studied *P. aeruginosa* strains.

This study was supported by grants PID2024-158933OB-I00 funded by MCIN/AEI/10.13039/501100011033 and "ERDF A way of making Europe"; the CERCA programme and AGAUR-Generalitat de Catalunya (grant number 2021SGR01545), by the European Regional Development Fund (FEDER) and the Catalan Cystic Fibrosis association. E.T. is a researcher of the ICREA Academia 2025 program. A.C.S is supported by a predoctoral fellowship funded by the Spanish State Research Agency (AEI) (Grant PREX2023-000036, funded by MICIU/AEI/10.13039/501100011033). A.R. is thankful to Generalitat de Catalunya for its financial support through FI (2025 FI-1 00583).

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 20 presented by:

NAME: Albert Ripoll

Enhanced Colistin Penetration Through Nanoparticle Encapsulation and Biofilm-Dispersing Enzymes to Treat Chronic Bacterial Infections

Albert Ripoll[1,2], Núria Blanco-Cabra[1,2], Raphaëlle Palau[1], José Carlos Ibáñez[3], Damien Lupin[3], Roger Fàbrega Alsina[4,5], Laura Molero Solís[4,6], Laia Montell Bonaventura[4], Iraida Loinaz[3], Eduard Torrents[1,2]

[1] Bacterial Infections: Antimicrobial Therapies, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology, Barcelona, Spain.
[2] Microbiology Section, Department of Genetics, Microbiology and Statistics, Faculty of Biology, University of Barcelona, 643 Diagonal Ave., 08028, Barcelona, Spain.
[3] CIDETEC, Basque Research and Technology Alliance (BRTA), Parque Científico y Tecnológico de Gipuzkoa, Donostia-San Sebastián, Spain.
[4] Reig Jofre Laboratories, Barcelona, Spain.
[5] Nanobioengineering Group, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain
[6] Department of Biochemistry and Molecular Biomedicine, School of Biology, University of Barcelona, Spain

Pseudomonas aeruginosa's biofilms are closely associated with persistent respiratory infections, especially in chronic lung diseases such as cystic fibrosis and chronic obstructive pulmonary disease (COPD), where they contribute to sustained inflammation and increased antibiotic tolerance. These biofilms pose a significant therapeutic challenge due to their dense extracellular matrix (ECM), which limits antibiotic penetration and promotes tolerance.

Colistin, a cationic polymyxin, can become trapped in the outer layers of the biofilm due to ionic interactions with anionic components of the ECM, such as extracellular DNA (eDNA) and alginate, reducing its antimicrobial efficacy.

In this work, we designed single-chain dextran-based nanoparticles loaded with colistin (SCPNs) that reduce ionic interactions between colistin and the ECM, thereby promoting greater penetration of the antibiotic into the biofilm. To further enhance anti-biofilm activity, the SCPNs were combined with two alginate lyases, A1-II' and Alg2A, previously described for their ability to degrade the alginate present in the biofilm matrix.

Our findings demonstrate that SCPNs loaded with colistin are more effective than free soluble colistin in mature mucoid *P. aeruginosa* biofilms grown under both static and continuous conditions, as well as in dynamic biofilms formed by non-mucoid clinical strains. Additionally, combining antibiotics with alginate lyases markedly enhanced the anti-biofilm effectiveness of colistin-loaded SCPNs. This effect led to a synergistic anti-biofilm response, demonstrated by a larger reduction in biofilm biomass and higher bacterial cell death rates in both mucoid and non-mucoid biofilms. Furthermore, colistin penetration across mature *P. aeruginosa* biofilms was measured by comparing free colistin to colistin-loaded SCPNs and their respective combinations with A1-II' and Alg2A alginate lyases, demonstrating better colistin penetration in the SCPN form and an overall improvement of colistin recovery when alginate lyases were used.

This study was supported by grant PID2024-158933OB-I00 funded by MCIN/AEI/ 10.13039/501100011033 and "ERDF A way of making Europe"; the CERCA programme and AGAUR-Generalitat de Catalunya (grant number 2021SGR01545), by the European Regional Development Fund (FEDER) and the Catalan Cystic Fibrosis association. E.T. is a researcher of the ICREA Academia 2025 program. A.R. is thankful to Generalitat de Catalunya for its financial support through FI (2025 FI-1 00583).

POSTER 21 presented by:
NAME: Alice Lissmatz

Mapping The Mutational Landscape Of Gelsolin D2 Amyloid Aggregation

Alice Lissmatz[1], Mariano Martín[1], Benedetta Bolognesi[1]

[1] Protein Phase Transitions in Health and Disease Research Group Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

Hereditary gelsolin amyloidosis (AGel amyloidosis) is a disease where proteolytic fragments of the gelsolin D2 domain, known as 8kDa and 5kDa fragments, form amyloid deposits in the cornea, liver and other tissues. The proposed molecular mechanism behind pathogenicity consists of the destabilization of the gelsolin D2 domain by mutations, increasing susceptibility to proteolytic cleavage and subsequent aggregation of the generated fragments. However, this mechanism has been debated and the effect of mutations on the aggregation propensity of these fragments is still poorly understood.

Here, we employ deep mutational scanning coupled to an aggregation reporter to investigate the effects of 608 single amino-acid mutations on amyloid aggregation in three different contexts: the whole D2 domain, and the 8kDa and 5kDa fragments.

Our results reveal that mutations can increase the aggregation propensity of the gelsolin D2 domain as well as that of 8kDa and 5kDa. This unprecedented gelsolin mutational atlas agrees with clinical data, showing the well-documented familial pathogenic variant D214N mutation as one of the strongest aggregators across different contexts. We also find 26 mutations with effects on aggregation comparable to or greater than that of D214N in the context of the full D2 domain. Most of these mutations show similar effects in 8kDa and 5kDa and may therefore represent potential pathogenic variants.

Furthermore, we identify D214 and D219 as candidate gatekeeper residues: most of the mutations at these positions dramatically increase amyloid aggregation. These two residues flank what has been reported as the minimal aggregating unit and are also positioned at opposite ends of β-strand-3 in the D2 domain.

Further studies into the cross-talk between mutational effects, protein destabilization and aggregation are needed to fully understand the molecular mechanisms involved in AGel amyloidosis. However, the gelsolin mutational atlas we present here is already a valuable resource for variant interpretation, with potential application for the clinical diagnosis and management of this disease.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 22 presented by:

NAME: Anna Griego

An AUTOTAC-Inspired Nanoparticle Strategy to Promote Host-Driven Clearance of *Pseudomonas aeruginosa*

Anna Griego[1], Ilaria Porello[1], Valentino Barbieri[1], Vanina Cosenza[1], Nuria Blanco Cabra[2], Eduard Torrents Serra[2] and Giuseppe Battaglia[1,3]

[1] Molecular Bionics Group, Institute for Bioengineering of Catalonia (IBEC), 08028 Barcelona, Spain.

[2] Bacterial Infections: Antimicrobial Therapies, Institute for Bioengineering of Catalonia (IBEC), 08028 Barcelona, Spain.

[3] Catalan Institution for Research and Advanced Studies (ICREA), 08010 Barcelona, Spain.

Chronic and recurrent bacterial infections remain a major clinical challenge because pathogenic bacteria can persist despite antibiotic treatment and exploit host-cell environments that are poorly accessible to conventional therapies. *Pseudomonas aeruginosa* is a highly adaptable opportunistic pathogen associated with difficult-to-treat infections, particularly in immunocompromised patients and in biofilm-prone or chronically inflamed tissues. Current antimicrobial strategies mainly aim to kill or inhibit bacteria directly, but this selective pressure can favour resistance and does not necessarily restore defective host clearance mechanisms. Therefore, alternative host-directed approaches are needed to enhance the ability of infected cells to recognise, process and eliminate bacterial materials.

This project aims to develop a modular host-directed platform that couples bacterial recognition with autophagy pathway engagement. Inspired by AUTOTAC-like strategies, we hypothesize that a synthetic probe combining a *P. aeruginosa*-binding module with an autophagy-targeting ligand could promote recruitment of p62/SQSTM1-dependent degradation pathways toward bacterial targets. In the final design, this probe will be incorporated into PMPC-PDPA-based nanoparticles to improve its delivery, stability and cellular uptake, while allowing multivalent presentation and local enrichment of the autophagy-recruiting signal.

As a first step toward this platform, we initiated the identification of *P. aeruginosa*-binding elements using phage display against a laboratory (PAO1) and clinical *P. aeruginosa* (PAET1) strains. This approach is intended to generate peptide ligands that can provide bacterial specificity to the final probe. Second, we evaluated the biological activity of the autophagy-targeting ligand YTK-105. In lung epithelial cells, soluble YTK-105 did not show a cytotoxic effect at the concentration tested and induced changes compatible with p62-associated autophagy modulation, such as increased p62 puncta formation by immunofluorescence. Thus, these preliminary data support the use of YTK-105 as the autophagy-engaging component of the AUTOTAC-like probe.

To explore nanoparticle-based delivery, in parallel, we started to develop an initial PMPC-PDPA formulation using film hydration. Preliminary results indicate that PMPC-PDPA nanoparticles can be used as a starting formulation strategy, although encapsulation efficiency, polymer recovery and particle homogeneity still require further optimisation.

Overall, we have validated YTK-105 activity in a relevant cellular context, initiated the discovery of *P. aeruginosa*-binding ligands, and generated an initial nanoparticle formulation pipeline for autophagytargeting cargo delivery. Ultimately, this project aims to provide a new antibacterial strategy that does not rely solely on direct bacterial killing but instead rewires host-cell degradation pathways to promote selective bacterial clearance.

POSTER 23 presented by:
NAME: Carles Prado Morales

SkinBots for the topical delivery of antigens

Carles Prado-Morales, Taco Waaijman, Inés Macías-Tarrío, Cristián Huck-Iriart, Tiziana Russo, Joël Gálvez-Savoca, Cesar Rodriguez-Emmenegger, Jasper J. Koning, Samuel Sánchez**

Current vaccination strategies primarily rely on injectable administration targeting tissues with relatively low densities of antigen-presenting cells (APCs), resulting in limited efficiency, reduced patient compliance, increased infection risk, and higher healthcare costs. In contrast, the skin contains a dense network of resident APCs, making it an attractive target for vaccination. However, most topical delivery approaches require physical disruption of the stratum corneum (SC) to overcome the skin barrier, often causing adverse effects and local tissue damage. To address these limitations, we have developed a novel needle-free delivery platform based on enzymatically powered nanomotors capable of actively and non-disruptively penetrating the skin barrier. The ability of these nanomotors to penetrate the skin was investigated using reconstructed human skin models. We elucidated how through self-propulsion and local modulation of the lipid organization of the SC, these nanomotors enhance transport into the viable epidermis and dermis.[1] Having established the potential of nanomotors as topical delivery vehicles, we subsequently loaded them with ovalbumin (OVA), which was used as a model antigen. In parallel, two types of skin-resident APCs, immature dendritic cells (iDCs) and immature Langerhans cells (iLCs), were generated through the differentiation of MUTZ-3 monocytes. The resulting cell models were characterized by quantifying the expression of CD1a, DC-SIGN, and Langerin. We further evaluated the biocompatibility of the nanomotor-based system and confirmed its internalization by monocytes. Future studies will determine whether these antigen-loaded nanomotors can efficiently activate skin-resident APCs, thereby assessing their potential as a novel platform for needle-free topical vaccination.

[1] Carles Prado-Morales, Taco Waaijman, Inés Macías-Tarrío, Cristián Huck-Iriart, Tiziana Russo, Joël Gálvez-Savoca, Cesar Rodriguez-Emmenegger, Jasper J. Koning, Samuel Sánchez; Enhancing Human Skin Penetration with Biodegradable Enzymatic Nanomotors. *ACS Nano* 2026; 20 (32): 23013–23033. https://doi.org/10.1021/acsnano.6c11619

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 24 presented by:

NAME: Carles Verdaguer

Developing a multicellular 3D *in vitro* model for the detection of high-performing iPSC-derived CAR-NK against HER2+ solid tumors

Carles Verdaguer[1,2,3], Sergi Casellas[1], Kenia Rodríguez[2], Karine Tadevosyan[2], Ana-Belén Álvarez[2], Xavier Rovira[1]

[1] Institute for Bioengineering of Catalonia (IBEC)

[2] Banc de Sang i Teixits (BST)

[3] Department of Biomedicine, University of Barcelona, Barcelona, Spain

Chimeric Antigen Receptor (CAR)-Natural Killer (NK) cells are promising candidates for cancer treatment, especially for hematological malignancies, with advantages including a lower risk of graft-versus-host disease, cytokine release syndrome, and neurotoxicity compared to T cells, supporting their use as allogeneic and off-the-shelf therapies. However, their use against solid tumors remains challenging, in part because of physical barriers of the extracellular matrix, immunosuppressive signals, hypoxia, among other aspects. We hypothesize that a defined combination of cytokines will boost CAR-NK efficacy, infiltration, and persistence. However, current in vitro models limit the capacity of testing therapies in a high throughput manner with a physiologically relevant set up. The aim of the project is to characterize the infiltration and cytotoxic activity of tens of CAR-NK variants in complex 3D in vitro models. As a first step, we generated MCF7 spheroids and tested cord blood NK cell infiltration in different ratios and timepoints to assess the dynamics of the infiltration using a simple model, observing presence of cord blood NK cells at 48h. Because of the complexity of the natural tumor microenvironment, we set up a heterogeneous model consisting of macrophages derived from THP-1 monocytic cell line, HCC2218 cell line as a cancer associated fibroblast, MCF7 cells expressing the p95HER2 antigen (a truncated variant of HER2 highly specific of esophageal and breast cancer) and supplemented with collagen that acts as an extracellular matrix component. In parallel, we are optimizing a protocol to provide a robust source of cytotoxic iNK cells. In the future, we will use this heterogeneous model to investigate how soluble factors, including cytokines and chemokines, regulate NK cell migration and infiltration into tumor spheroids. It will provide a controlled platform to dissect the complex signaling networks governing NK cell behavior within the tumor microenvironment, identify strategies to improve NK cell activity against HER2-positive and other solid tumors, and support the development of more effective NK cell-based therapies.

POSTER 25 presented by:

NAME: Daniela Currea

Unravelling the Molecular Targets and Mode of Action of Compound EMA377 in *Leishmania infantum*

Daniela Currea-Ayala[1,2,3], Ana Victoria Ibarra-Meneses[4, 5] Lucía Román-Álamo[1,2], Elsa M. Arce[6], Diego Muñoz-Torrero[6,7], Christopher Fernández-Prada[4,5], Yunuen Avalos- Padilla[1,2], Xavier Fernàndez-Busquets[1,2,8]

[1] Barcelona Institute for Global Health (ISGlobal), Hospital Clínic-Universitat de Barcelona, Parc Científic de Barcelona, Baldiri Reixac 10-12, 08028 Barcelona, Spain.

[2] Nanomalaria Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology, Baldiri Reixac 10-12, 08028 Barcelona, Spain.

[3] Doctoral School of Biotechnology, Faculty of Pharmacy and Food Sciences, University of Barcelona, 08028 Barcelona, Spain.

[4] The Research Group on Infectious Diseases in Production Animals (GREMIP), Faculté de Médecine Vétérinaire, Université de Montréal, Saint-Hyacinthe, QC, Canada

[5] Département de Pathologie et Microbiologie, Faculté de Médecine Vétérinaire, Université de Montréal, Saint-Hyacinthe, QC, Canada

[6] Laboratory of Medicinal Chemistry, Faculty of Pharmacy and Food Sciences, University of Barcelona, Av. Joan XXIII 27-31, 08028 Barcelona, Spain

[7] Institute of Biomedicine (IBUB), University of Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain

[8] Nanoscience and Nanotechnology Institute (IN2UB), University of Barcelona, Martí i Franquès 1, 08028 Barcelona, Spain.

Leishmaniasis is a parasitic disease caused by protozoa of the genus *Leishmania*. It causes nearly 1 million new cases annually across 100 endemic countries, with significant implications not only for human health but also for veterinary medicine, with the disease frequently affecting dogs. Current therapies are limited by non-specific toxicity, invasive administration, and the emergence of drug resistance. Moreover, climate change is expanding both the geographical range and the seasonality of *Leishmania* vectors, thereby turning leishmaniasis into an emerging disease in previously non-endemic regions. Consequently, there remains an urgent need for new compounds that directly target the parasite. To address this gap, we are describing a new family of antileishmanial compounds. YAT2150 is a compound first described against *Plasmodium falciparum* that shows a potent antileishmanial activity, but a high non-specific toxicity. Its derivative, EMA377 retains the potent antileishmanial activity with reduced toxicity. To describe the mode of action of this compound in *Leishmania infantum*, we are identifying its molecular targets through an integrated approach that includes transcriptomics, cellular thermal shift assays (CETSA), and a stepwise selection of resistant lines followed by their wholegenome sequencing. Additionally, resistant clones are being further characterized to assess fitness costs and cross-resistance profiles. Candidate targets were prioritized by reproducibility and thermal shift magnitude, and are being validated via overexpression lines. Preliminary analyses indicate that EMA377 disturbs diverse molecular processes, especially metabolic and redox pathways, showing multiple protein targets. EMA377 is a promising, low-toxicity candidate that directly targets several essential parasite pathways. Defining its mode of action will strengthen our knowledge about this family of compounds and will bring us one step closer to optimizing these molecules, anticipating resistance mechanisms, and advancing them towards clinical development.

This work was supported by grant PID2024-156230OB-I00, funded by *Ministerio de Ciencia, Innovación y Universidades/Agencia Estatal de Investigación* (MCIU/AEI/ 10.13039/501100011033), which included FEDER and European Union NextGenerationEU/PRTR funds.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 26 presented by:

NAME: Dayaneth Jácome Montero

From Brain to Blood: Evaluation of miR-519a-3p as a Minimally Invasive Biomarker for Alzheimer's Disease

Dayaneth Jácome[1,2], José Antonio del Río[1,2,3,4], Rosalina Gavín[1,2,3,4]

[1] Molecular and Cellular Neurobiotechnology, Institute for Bioengineering of Catalonia, Barcelona, Spain.
[2] Department of Cell Biology, Physiology and Immunology, University of Barcelona, Barcelona, Spain.
[3] Institute of Neuroscience, University of Barcelona, Barcelona, Spain.
[4] Center for Networked Biomedical Research in Neurodegenerative Diseases (CIBERNED), Barcelona-Madrid, Spain.

Our previous studies identified miR-519a-3p as a regulator of *PRNP* expression and demonstrated its early upregulation in Alzheimer's disease (AD) brain tissue, including asymptomatic cases, supporting its potential as an early disease biomarker. The primary objective of the present work was to evaluate the feasibility of detecting miR-519a-3p in blood-derived samples and to explore its potential clinical utility in different AD-related populations. To this end, we optimized and implemented a robust RT-qPCR-based protocol for the quantification of miR-519a-3p in both plasma and serum samples. Successful detection was achieved in both biological matrices, representing an essential step towards the development of a minimally invasive biomarker.

Preliminary analyses were performed in three independent cohorts. The first cohort included patients with clinically diagnosed AD, the second comprised individuals in preclinical stages of the disease, and the third consisted of first-degree relatives of AD patients enrolled in a longitudinal follow-up study with clinical, cognitive, and biochemical assessments. Although the sample size is still limited and ongoing recruitment and analysis are expected to strengthen the conclusions, miR-519a-3p was consistently detected in all three cohorts. In patients with established AD, circulating miR-519a-3p levels showed an association with disease progression, supporting previous observations linking this miRNA to AD pathology. In preclinical and familial cohorts, the availability of longitudinal data and biomarkers enabled exploratory analyses to assess whether miR-519a-3p levels might be associated with established AD-related markers, yielding preliminary observations that warrant further investigation.

Taken together, these results demonstrate the feasibility of measuring miR-519a-3p in plasma and serum and provide preliminary evidence supporting its potential value as a blood-based biomarker across different stages of the Alzheimer's disease continuum. Ongoing analyses in expanded cohorts will determine its utility for early detection, risk stratification, and disease monitoring.

POSTER 27 presented by:

NAME: Dunja Arsenijevic

Exploring the interactions of small-molecule probes with protein condensates as a potential targeting mechanism in *Plasmodium falciparum*

Dunja Arsenijević[1,2], Elias Sabri[3], Elsa M. Arce[4,5], Ana Mallo-Abreu[4,5], Diego Muñoz-Torrero[4,5], Rumiana Dimova[3], Yunuen Avalos Padilla[1,2], Xavier Fernàndez-Busquets[1,2]*

[1] *Barcelona Institute for Global Health (ISGlobal, Hospital Clínic-University of Barcelona), Rosselló 149-153, 08036 Barcelona, Spain.*
[2] *Nanomalaria Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology, Baldiri Reixac 10-12, 08028 Barcelona, Spain.*
[3] *Max Planck Institute of Colloids and Interfaces, Science Park Golm, 14476 Potsdam, Germany.*
[4] *Laboratory of Medicinal Chemistry, Faculty of Pharmacy and Food Sciences, University of Barcelona, Av. Joan XXIII, 27-31, 08028 Barcelona, Spain.*
[5] *Institute of Biomedicine (IBUB), University of Barcelona, Av. Diagonal 643, 08028, Barcelona, Spain.*

The formation of biomolecular condensates via liquid-liquid phase separation (LLPS) has emerged as a key regulatory mechanism of cellular processes. While the current understanding of condensate biology is based on yeast and mammalian cell models, little is known about their biological function in protozoan parasites. Plasmodium falciparum, the deadliest species of the parasite causing human malaria, is exposed to significant temperature changes during its complex life cycle, experiencing conditions that have been reported to cause condensate formation in other organisms. Preliminary observations in P. falciparum suggest that biomolecular condensates serve both as fundamental organizational units in essential cellular processes and as stress-induced adaptive assemblies. However, their functional role and therapeutic targetability remain largely unexplored.

We have identified the aggregated protein dye YAT2150 as a highly potent antimalarial compound. While its precise mechanism of action remains unclear, evidence suggests that YAT2150 may interact with structurally disordered protein regions, potentially targeting key cellular processes in the parasite. Despite its potency, low likelihood of resistance evolution, and cost-efficiency, its therapeutic window remains limited due to relatively high cytotoxicity in human cells, prompting the synthesis and evaluation of chemical analogues.

Within this chemical family, we identified compounds that accumulate in discrete condensate-like structures in live P. falciparum parasites. To examine whether their tendency to partition inside condensates is independent from the complex cellular context, and controllably screen different types of molecule-condensate interactions, we established a minimal reconstituted in vitro system based on a variety of phase-separating proteins encapsulated in giant unilamellar vesicles. The YAT2150-related compounds partitioned to protein condensates, indicating that their behavior is governed by conserved physicochemical properties rather than organism- or protein-specific factors. However, quantitative partitioning assays in condensates hint at the importance of the small molecule probe's chemical structure that may be exploitable for therapeutic targeting in the malaria parasite.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 28 presented by:

NAME: Guanyu Zhou

Engineering Multivalent ApoE Nanostructures for Isoform-Dependent Neurovascular Unit Reprogramming

Guanyu Zhou[1,2], Anna Griego[1], Adriano Caliari[1], Vanina Cosenza[1], Lorena Ruiz-Perez[1,2], Giuseppe Battaglia[1,3]

[1] Molecular Bionics Group, Institute for Bioengineering of Catalonia (IBEC), C. Baldiri Reixac 10–12, 08028 Barcelona, Spain.
[2] Department of Applied Physics, Faculty of Physics, University of Barcelona, 08028 Barcelona, Spain.
[3] Catalan Institution for Research and Advanced Studies (ICREA), 08010 Barcelona, Spain.

Neurovascular unit (NVU) dysfunction, including blood-brain barrier (BBB) hyperpermeability, impaired cerebral blood flow, and dysregulated communication between vascular and glial cells, is increasingly recognised as an early and disease-amplifying feature of major neurodegenerative disorders, particularly Alzheimer's disease(AD) [1]. Apolipoprotein E (ApoE), the principal regulator of cerebral lipid transport, exists in three major human isoforms (ApoE2, ApoE3, and ApoE4) that differ at residues 112 and 158, influencing ApoE conformation, lipid interactions, and self-association, thereby contributing to their divergent effects on brain homeostasis [2]. While ApoE3 represents the most common isoform and physiological reference and ApoE2 is associated with lower AD risk, ApoE4 is the strongest genetic risk factor for AD, actively driving early BBB breakdown, microvascular degeneration, and pro-inflammatory glial activation [3]. We hypothesize that these isoform-dependent effects are shaped not only by ApoE sequence, but also by how ApoE is spatially presented at the nanoscale. Previous research in the group demonstrates that the ApoE receptor, Low-density lipoprotein receptor-related protein-1 (LRP1), regulates trafficking across the BBB depending on cargo avidity. High-avidity structures are internalized into endo-lysosome networks for degradation, while mid-avidity structures are transported across the endothelium via tubular vesicles stabilized by sydapin-2 proteins. This has been observed for both synthetic nanoparticles [4] and amyloid beta aggregates [5]. Importantly, we found that the syndapin-2 LRP1 pathway is linked to full vascular function recovery, offering a promising therapeutic opportunity for AD treatment [6].

We suggest that ApoE morphological geometry and surface density regulate receptor clustering and trafficking, thereby modulating downstream vascular and glial responses. To test this hypothesis, we will compare high-density lipoprotein (HDL)-like nanodiscs with lipid-droplet mimetics designed to have larger diameters than the nanodiscs, enabling us to disentangle the respective contributions of isoform, nanoscale organization, and ligand density to NVU signalling. Full-length ApoE2, ApoE3, and ApoE4 will be recombinantly produced in a mammalian expression system, biochemically validated, and purified by affinity chromatography. Recombinant ApoE isoforms will be used to establish and optimize lipidation protocols for their incorporation into defined HDL-like nanodiscs and lipid-droplet mimetics. We have successfully established the production and purification of recombinant ApoE4. Initial biophysical characterization revealed the formation of higher-order ApoE assemblies in solution, highlighting the importance of controlling lipidation and nanoscale organization for subsequent platform development.Further biophysical characterization will be used to resolve solution-state size populations and guide lipidation. Reconstitution protocols will then generate defined ApoE-presenting HDL-like nanodiscs and lipid-droplet mimetics with controlled size and surface composition. These platforms will be evaluated in human BBB-on-a-chip and glial co-culture models to quantify barrier integrity, receptor organization and trafficking, and cellular inflammatory responses.

References

[1] Zlokovic BV. The blood-brain barrier in health and chronic neurodegenerative disorders. Neuron. 2008;57(2):178–201. doi:10.1016/j.neuron.2008.01.003.

[2] Liu C-C, Kanekiyo T, Xu H, Bu G. Apolipoprotein E and Alzheimer disease: risk, mechanisms and therapy. Nat Rev Neurol. 2013;9(2):106–118. doi:10.1038/nrneurol.2012.263.

[3] Montagne A, Nation DA, Sagare AP, et al. APOE4 leads to blood–brain barrier dysfunction predicting cognitive decline. Nature. 2020;581(7806):71–76. doi:10.1038/s41586-020-2247-3.

[4] Tian X, Leite DM, Scarpa E, et al. On the shuttling across the blood-brain barrier via tubule formation: mechanism and cargo avidity bias. Sci Adv. 2020;6(48):eabc4397. doi:10.1126/sciadv.abc4397.

[5] Leite DM, Seifi M, Ruiz-Perez L, et al. Syndapin-2 mediated transcytosis of amyloid-β across the blood-brain barrier. Brain Commun. 2022;4(1):fcac039. doi:10.1093/braincomms/fcac039.

[6] Chen J, Xiang P, Duro-Castano A, et al. Rapid amyloid-β clearance and cognitive recovery through multivalent modulation of blood-brain barrier transport. Signal Transduct Target Ther. 2025;10(1):331. doi:10.1038/s41392-025-02426-1.

POSTER 29 presented by:

NAME: Ilaria Porello

Phosphorylcholine-presenting polymer micelles with intrinsic anti-inflammatory activity via scavenger receptor engagement

Ilaria Porello[1,2], Matilde Ghibaudi[2], Vanina Cosenza[2], Valentino Barbieri[2], Francesco Cellesi[1], Giuseppe Battaglia[2,]*

[1] Department of Chemistry, Materials and Chemical Engineering "G. Natta", Politecnico di Milano, Via Luigi Mancinelli 7, 20131, Milan, Italy.

[2] Institute for Bioengineering of Catalonia (IBEC), Carrer de Baldiri Reixac 10-12, 08028, Barcelona, Spain.

Engineering nanoparticles that combine targeted receptor engagement with intrinsic bioactivity represents a key challenge in modern therapeutic strategies. This work presents amphiphilic diblock copolymers composed of poly(ε-caprolactone) and poly(2-methacryloyloxyethyl phosphorylcholine) (PCL-*b*-PMPC) that self-assemble into nanoparticles designed to engage scavenger receptors SR-B1, CD36, and CD81, thereby modulating anti-inflammatory and cytoprotective pathways. By systematically varying the lengths of the hydrophobic PCL and hydrophilic PMPC blocks while maintaining a constant hydrophilic/hydrophobic ratio, precise control over nanoparticle size, morphology, and PMPC surface density was achieved. This revealed that receptor-mediated uptake and functional outcomes strongly depend on PMPC chain length. The nanoparticles displayed homogeneous micellar conformation, ensuring good colloidal stability and low cytotoxicity, while effectively reducing ROS levels in LPS-stimulated microglia. The activation of the Nrf2 antioxidant pathway in HepG2 ARE^{+} cells further supports the mechanism of action of PMPC, in contrast to bioinert poly(ethylene glycol)-based micelles, which exhibit no activity in this context. These results establish PCL-*b*-PMPC nanoparticles as a tunable platform for targeted modulation of inflammation and oxidative stress, offering a promising strategy for next-generation nanotherapeutics.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 30 presented by:

NAME: Inés Macías Tarrío

Nanomotors-mediated delivery of FGFR3 inhibitor for bladder cancer therapy

Inés Macías-Tarrío[1,2], Núria Sabando-García[3], Kristin Fichna[1,2], Acsah Konuparamban[4], Noemí Traba[3], Carles Prado-Morales[1,2], Marc Armengol[5], Rosa M. Rabanal[6], Florencia Lezcano[1], Oriol Jutglar[1], Silvia Lope-Piedrafita[7,8,9], Valerio Di Carlo[1], Jordi Llop[4], Esther Julián[3]*, Samuel Sánchez[1,10]**

[1] *Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Baldiri i Reixac 10-12, 08028 Barcelona, Spain*

[2] *Departament de Bioquímica i Fisiologia, Facultat de Farmàcia i CCAA, Universitat de Barcelona Av. Joan XXIII, 27-31, 08028-Barcelona*

[3] *Departament de Genètica i de Microbiologia, Facultat de Biociències, Universitat Autònoma de Barcelona, 08193, Cerdanyola del Vallès, Spain*

[4] *CIC biomaGUNE, Basque Research and Technology Alliance (BRTA), Paseo Miramón 182, 20014, Donostia/San Sebastián, Spain*

[5] *Nanobots Therapeutics S.L., Baldiri i Reixac 10-12, 08028, Barcelona, Spain*

[6] *Unitat de Patologia Murina i Comparada, Department of Animal Medicine and Surgery, Veterinary Faculty, Universitat Autònoma de Barcelona, 08193, Cerdanyola del Vallès, Spain*

[7] *Unitat de Biofísica, Departament de Bioquímica i Biologia Molecular, Facultat de Medicina, Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallès, Spain*

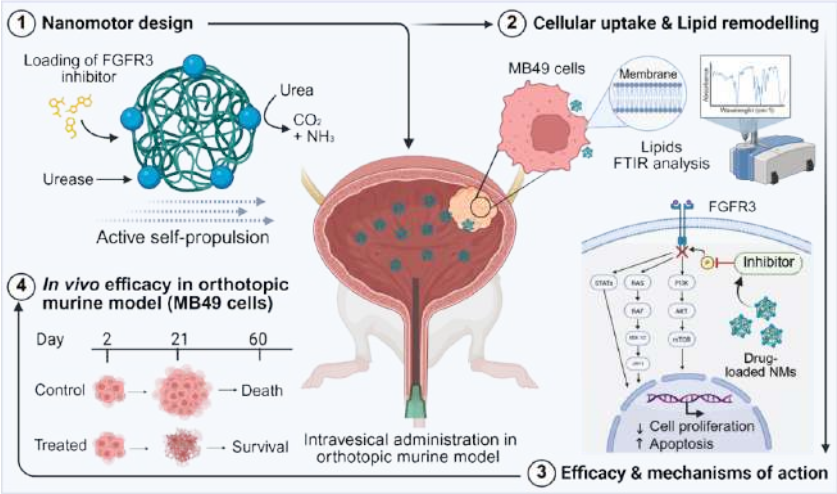
[8] *Servei de Ressonància Magnètica Nuclear, Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallès, Spain*

[9] *Centro de Investigación Biomédica en Red-Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Universitat Autònoma de Barcelona, 08193 Cerdanyola del Vallès, Spain*

[10] *Institució Catalana de Recerca I Estudis Avançats (ICREA), Passeig Lluís Companys 23, 08010 Barcelona, Spain*

Non-muscle-invasive bladder cancer (NMIBC) represents a major clinical challenge due to its high rate of recurrence and the persistent risk of disease progression, despite generally favorable long-term outcomes. The effectiveness of intravesical chemotherapy is often compromised by rapid elimination of therapeutics through urination, limited penetration into tumor tissue, and inadequate retention caused by particle sedimentation. Urease-driven NMs offer a potential solution to these limitations by converting endogenous urea into propulsion, thereby promoting active movement, improving drug distribution, and enhancing interactions with tumor cells. Nevertheless, existing urease-powered systems have predominantly been developed using inorganic materials and have largely incorporated nonspecific therapeutic agents, with limited consideration of the molecular heterogeneity underlying NMIBC such as alterations in fibroblast growth factor receptor 3 (FGFR3), which occur in approximately 60-70% of NMIBC cases. In this study, we developed a biodegradable, enzymatic NMs designed to exploit FGFR3 signaling for targeted NMIBC treatment. Biocompatible poly(lactic-co-glycolic acid) (PLGA) NMs were functionalized with urease and encapsulated with the FGFR3 inhibitor, generating FGFR3Inh@NMs. Urease-mediated propulsion significantly improved NM diffusion and promoted their uptake by bladder cancer cells. Mechanistic studies in vitro demonstrated that FGFR3Inh@NMs promoted S-phase cell-cycle arrest and triggered apoptosis. Notably, NM-mediated delivery increased drug efficiency, resulting in an approximately 10-fold reduction in the IC_{50} compared with administration of the free drug. Furthermore, intravesical treatment with FGFR3Inh@NMs in an orthotopic mouse model of NMIBC markedly inhibited tumor progression, reduced disease recurrence and presented a 83% of survival compared with no survival in control mice. Collectively,

these results support urease-powered NMs as a promising delivery system for intravesical targeted therapy in NMIBC.



POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 31 presented by:

NAME: Kristin Fichna

Nanomotor-Driven Transport Potentiates ADC Efficacy Across Target Heterogeneity

Kristin Fichna [†,1,2], Valerio Di Carlo[1], Oriol Jutglar Soler[1], Shuqin Chen[1], Olivier Van Kerk[3], Ludovic Bigot[4], Yohann Loriot[4], Kristine Schauer [5,6], Emna Ouni[,†,5] & Samuel Sanchez[*,1,7]*

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Baldiri i Reixac 10-12, 08028 Barcelona, Spain

[2] Doctorate in Biotechnology, Facultat de Farmàcia i Ciències de l'Alimentació, Universitat de Barcelona, Avda. Diagonal 643, 08028 Barcelona, Universitat de Barcelona, Spain

[3] Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain, Brussels, Belgium

[4] Biomarqueurs prédictifs et nouvelles stratégies thérapeutiques en oncologie, Inserm U981, Gustave Roussy Cancer Center, Université Paris-Saclay, Villejuif, France

[5] Tumor Cell Dynamics Unit, Inserm U1279 Gustave Roussy Institute, Université Paris-Saclay, Villejuif, France

[6] Centre National de la Recherche Scientifique (CNRS), Villejuif, France

[7] Institució Catalana de Recerca I Estudis Avancats (ICREA), 08010 Barcelona, Spain

[†]Equal contribution

Antibody-drug conjugates (ADCs) have transformed the treatment of advanced urothelial carcinoma, yet their efficacy can be limited by poor transport through tumor tissue. Enfortumab vedotin (EV), a Nectin-4-targeting ADC, shows clinical activity even in tumors with low target expression, while high Nectin-4 expression does not consistently predict treatment response, suggesting that factors beyond receptor abundance, including limitations in intratumoral drug delivery, influence the therapeutic outcome. Here, we investigated whether urease-powered nanomotors (NM) could enhance EV delivery by actively modifying the local transport environment by active fluid mixing. Biodegradable poly(lactic-co-glycolic acid) (PLGA) urease NM were co-administered with EV and evaluated in patient-derived xenograft (PDX) bladder cancer tumoroids spanning low, intermediate, and high Nectin-4 expression. Particle image velocimetry confirmed NM-driven fluid mixing, while fluorescence imaging and quantitative label-free holotomography enabled longitudinal assessment of NM and EV distribution, lysosomal processing, and treatment response. NM activation increased NM and EV penetration and accumulation within tumoroids and enhanced lysosomal EV processing, with increased lysosomal signals extending further into the tumoroid interior. These transport effects translated into enhanced therapeutic efficacy across all three patient-derived models. Together, these findings establish NM-driven fluid mixing as a strategy to overcome transport limitations of large biological therapeutics and potentiate ADC therapy without modifying the therapeutic itself.

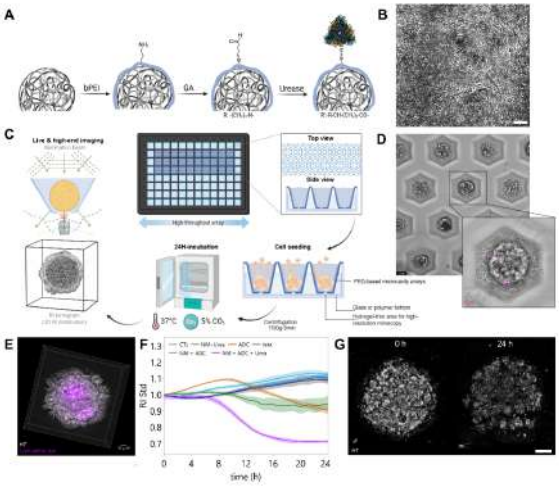


Figure 1. A) Schematic illustration of surface modification of PLGA nanoparticles to obtain urease-powered NM. Created in BioRender. Prado Morales, C. (2026). B) Scanning electron microscopy image of PLGA nanoparticles. C) Schematic illustration of the microcavity array design and workflow used to generate bladder PDX tumoroids for holotomography (HT) imaging and 3D reconstruction based on refractive index (RI) mapping. D) Overlay of brightfield observation of live tumoroids with internalized Cy-5-labeled active NM (100 mM urea). E) Three-dimensional (3D) projection of tumoroid with HT acquisition, conjugated to epifluorescent staining for visualization of ADC in lysosome (pink), following treatment during 4 h with ADC+NM+urea. F) Time-dependent evolution of RI Std in tumoroids, following treatment with free ADC, NM, NM+Urea, NM+ADC, or NM+ADC+Urea (100 mM urea). G) Representative maximum-intensity projection images of tumoroids at selected time points (0h, 24 h) after treatment withADC+NM+urea.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 32 presented by:

NAME: Lucia Roman

YAT2150 Analogues Target Stress-Induced Molecular Condensates in *Leishmania infantum*

Lucía Román Álamo[1,2], Yunuen Avalos-Padilla[1,2], Daniela Currea-Ayala[1,2], Antonino Nicolò Fallica[1,2], Ana Mallo-Abreu[3,4], Elsa M. Arce[3,4], Diego Muñoz-Torrero[3,4], Xavier Fernàndez- Busquets[1,2]*

[1] *Nanomalaria Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology, Baldiri Reixac 10-12, 08028 Barcelona, Spain.*

[2] *Barcelona Institute for Global Health (ISGlobal, Hospital Clínic-University of Barcelona), Rosselló 149-153, 08036 Barcelona, Spain.*

[3] *Laboratory of Medicinal Chemistry, Faculty of Pharmacy and Food Sciences, University of Barcelona, Av. Joan XXIII, 27-31, 08028 Barcelona, Spain.*

[4] *Institute of Biomedicine (IBUB), University of Barcelona, Av. Diagonal 643, 08028 Barcelona, Spain.*

Leishmaniases comprise a spectrum of vector-borne diseases, including visceral (VL), cutaneous (CL), and mucocutaneous (MCL) forms, transmitted by phlebotomine sandflies and caused by kinetoplastid parasites of the genus *Leishmania*. The *Leishmania* life cycle unfolds between flagellated promastigotes within the insect vector and intracellular amastigotes in the mammalian host. Current World Health Organization estimates indicate a significant global burden, with approximately one million CL and 90,000 VL cases occurring annually. However, the existing drug arsenal is limited due to low efficacy and high systemic toxicity. Consequently, there is an urgent need to improve antileishmanial treatments by identifying new families of compounds and novel therapeutic targets to enhance safety profiles and ensure efficient activity.

Recently, our group identified a new compound, YAT2150, which demonstrated potent activity against *Leishmania infantum*, the species responsible for most leishmaniasis cases across the Mediterranean region. To improve the safety profile of YAT2150, several new analogues were synthesized, showing significantly reduced nonspecific toxicity *in vitro*. YAT2150 is the primary component of Proteostat, a commercial dye used to detect protein aggregation, which led us to use the intrinsic fluorescence of YAT2150 analogues to observe their distribution within the parasite with fluorescence microscopy.

Our preliminary results revealed that, under conditions of nutrient deprivation, the distribution of YAT2150 derivatives changed from a diffuse signal to the formation of bright and localized dots within the parasite. These findings suggest that the YAT2150 analogues are interacting with stress-induced condensates. We propose that these structures represent liquid-liquid phase separation (LLPS) events used by the parasite to survive environmental stress. Further research must be conducted to determine if the antileishmanial activity of this chemical family is related to the modulation of these molecular condensates. This study highlights the potential of YAT2150 analogues as both therapeutic agents and novel tools for studying phase separation in kinetoplastids.

The project that gave rise to these results has received funding from the “la Caixa” Foundation under grant agreement LCF/PR/HR24/52440003 (XF-B and DM-T) and from grant PID2024-156230OB-I00, funded by the *Ministerio de Ciencia, Innovación y Universidades/Agencia Estatal de Investigación* (MCIU/AEI/10.13039/501100011033).

POSTER 33 presented by:

NAME: Marta Badia Graset

Mapping distinct Aβ42 aggregation pathways for precision medicine

Marta Badia-Graset[1], Mireia Seuma[2], Sergi Tosal[1], André Ciupitu[3], Romain Pastre[4], Ben Lehner[2,4,5], Benedetta Bolognesi[1]

[1] *Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain*
[2] *ALLOX, Barcelona, Spain*
[3] *Université Libre de Bruxelles (ULB), Brussels, Belgium*
[4] *Center for Genomic Regulation (CRG), Barcelona, Spain*
[5] *Wellcome Sanger Institute, Hinxton, United Kingdom*

To date, 18 amyloid beta 42 (Aβ42) variants are linked to Alzheimer's disease, all accelerating amyloid formation. But do they all cause disease through a single mechanism? And are all mutations that accelerate amyloid formation pathogenic? Answering these questions is critical for accurate patient risk stratification and targeted therapy. Previously, we experimentally measured the amyloid formation of >2000 Aβ42 variants using a high-throughput yeast-based assay, identifying 314 variants that accelerate amyloid formation. This pool included known familial Alzheimer's disease (fAD) mutations alongside hundreds of previously uncharacterized variants.

To test if all accelerating variants share the same pathogenic route, we used intramolecular genetic interaction profiling. This rests on a core principle: variants that accelerate amyloid formation through the same molecular mechanism will respond similarly to secondary mutations. By introducing a panel of mutations in the Aβ42 core across 33 distinct Aβ42 variant backgrounds, we measured aggregation of >9000 double mutants and obtained an interaction profile for each Aβ42 variant, capturing how secondary mutations alter amyloid formation in each specific Aβ42 background.

Our interaction profiles stratified variants into two distinct classes. All known fAD mutations clustered together, pointing to a shared disease-driving mechanism, whereas a second group accelerated aggregation through an alternative pathway.

To uncover what sets these two classes apart, we modeled Aβ42 variants using AlphaFold3 and found that variants within the same mutational cluster shared higher structural similarity than those from different clusters. To test if these predictions reflected structural differences *in vivo*, we quantified >200 aggregate features and clustered Aβ42 variants by aggregate morphology. Comparing these morphological clusters back to our genetic profiles revealed a striking match, confirming that our mutational groups reflect fundamentally different structural arrangements.

This convergence across genetic maps, structural predictions, and aggregate morphology demonstrates that speeding up Aβ42 formation is not inherently pathogenic. By separating true fAD-like drivers from alternative accelerators, our platform lays out the groundwork for more precise pathogenicity assessments and targeted therapies.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 34 presented by:

NAME: Martín Ruiz Gutiérrez

Portable grating-coupled SPR platform using Blu-ray-based sensing chips for multiplexed biosensing

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

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain

Surface plasmon resonances (SPRs) are physical phenomena by which resonant electromagnetic waves couple and become collective oscillations of free electrons in metals. Biosensing using SPR requires the use of a metal, typically gold, whose free electrons will oscillate at the interface with a dielectric along which the resonance will propagate. This resonance evanescently penetrates the adjacent medium and is extremely sensitive to changes in the refractive index, which will be caused by biomolecular interactions. There are several configurations of SPR sensing platforms, including prism, waveguide, and grating coupled. The latter uses nanograting structures to achieve light coupling, increasing the complexity of the sensing chip but reducing the platform's. Here, we present a portable SPR sensing platform which includes the necessary components to perform sample injection experiments for the detection of biomolecules. The sensing principle is based on wavelength interrogation, using a lamp-based light source to illuminate the sensing spots of the chip through a collimator and a polarizer at a 45º angle of incidence. The reflected light is collected through another collimator and analyzed using a spectrometer. An integrated PC uses in-house developed software to track the minimum in the spectrum caused by the SPR effect, achieving real-time and label-free sensing. The sensing chip is mounted on a 2-position holder attached to a linear stage, allowing to scan sensing spots in parallel or in series. A 6-port injection valve is used to inject the sample into the system, with a custom in-line bubble trapper between the valve and the sensing chip. Alternatively, an organ-on-a-chip can be directly connected to the device through a microfluidic port for continuous sample monitoring. This platform provides a convenient setup to perform sensing experiments using SPR and is a step to bring this technology closer to point-of-care applications.

POSTER 35 presented by:

NAME: Núria Blanco-Cabra

A simple diagnostic platform reveals shear stress as critical in biofilm development

Núria Blanco-Cabra[1,2], José Huguet[3,4], Josep Samitier[3,4,5], Romén Rodríguez-Trujillo[3,4,5], Eduard Torrents[1,2].

[1] Bacterial Infections and Antimicrobial Therapies Group (BIAT), Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.

[2] Microbiology Section, Department of Genetics, Microbiology and Statistics, Faculty of Biology, University of Barcelona (UB), Barcelona, Spain.

[3] Nanobioengineering Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.

[4] Department of Electronics and Biomedical Engineering, Faculty of Physics, University of Barcelona (UB), Barcelona, Spain.

[5] Biomedical Research Networking Center in Bioengineering, Biomaterials, and Nanomedicine (CIBER-BBN), Av. Monforte de Lemos, 3-5, Pabellón 11, Planta 0, Madrid, Spain.

Chronic infections associated with biofilms display increased tolerance to antibiotics, highlighting the need for more accurate and personalized diagnostic approaches, as well as simple and accessible platforms for growing biofilms under controlled flow conditions that better mimic *in vivo* environments. The XpertBiofilm is a novel platform designed to reproduce dynamic flow conditions by applying controlled shear stress, enabling a more realistic simulation of biofilm formation while allowing straightforward downstream analysis. Using this platform, we demonstrated a direct relationship between shear stress and biofilm biomass formation in *Pseudomonas aeruginosa*. Moreover, the XpertBiofilm was successfully validated for diagnostic applications using both clinical *P. aeruginosa* strains and direct sputum samples from cystic fibrosis patients, accurately reflecting their known susceptibility profiles and supporting the platform's potential to enable better patient treatment selection. Overall, the XpertBiofilm provides a reliable, user-friendly, and physiologically relevant platform for studying biofilms and evaluating therapeutic strategies, offering strong potential for both basic research and personalized clinical diagnostics.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 36 presented by:

NAME: Samantha Morón Ros

3D-Bioprinting of functional β-cell spheroids for Type 1 Diabetes treatment

Samantha Morón-Ros[1]; Laurian de Vries[1]; Laura Clua-Ferré[1]; Natalia Castro[1]; Javier Ramón-Azcón[1,2].

[1] Institut de Bioenginyeria de Catalunya (IBEC). Barcelona, Spain.
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA). Barcelona, Spain.

Type 1 Diabetes Mellitus (T1DM) is characterized by an autoimmune-mediated destruction of pancreatic β-cells, resulting in absolute insulin deficiency. Patients depend on lifelong exogenous insulin therapy and must continually monitor their blood glucose to prevent serious complications. Current treatments cannot truly replicate the physiological insulin secretion of healthy β-cells. Cell-based therapies represent an emerging therapeutic frontier. Our innovative platform, UNIINK, addresses these unmet needs in cell therapy for T1DM. UNIINK enables rapid, sterile, and operator-independent fabrication of 3D bioprinted micro-spheroids, allowing normoglycemia restoration in T1DM patients. Our system allows scalable production using clinically validated materials: collagen I crosslinked with tannic acid (ColTA). This unique biomaterial overcomes the main limitations of existing cell therapies: enhanced structural integrity and resistance to enzymatic degradation, effective containment of cells within spheroids, optimal diffusion of nutrients and oxygen, immune protection of embedded cells, enabling insulin secretion while obviating the need for systemic immunosuppression. We successfully produced ColTA spheroids and demonstrated their long-term viability and functionality in vitro, maintaining β-cell survival and insulin secretion capacity for up to two months. In vivo studies further confirmed the translational potential of our technology. Spheroid transplantation into immunocompetent mice enabled the retrieval of intact spheroids without eliciting inflammatory response, as demonstrated through cytokine profiling and flow cytometry analyses. These results suggest that the biomaterial composition confers a degree of immune invisibility, supporting its use without systemic immunosuppression. To assess therapeutic efficacy, we tested the spheroids in hyperglycaemic mice. Notably, transplantation of INS1-E β-cell–laden spheroids led to substantial and sustained reductions in blood glucose levels. In treated animals, glycaemia decreased from severely hyperglycemic levels (>600 mg/dL) to near-physiological values (200–300 mg/dL). These promising results highlight the robustness, biofunctionality, and immunomodulatory properties of our UNIINK platform and support its further development toward clinical translation in T1DM therapy.

POSTER 37 presented by:

NAME: Sarahi Elizondo

Ionicombisomes: Synthetic Cells Across Mucus

Sarahi Marieliza Elizondo Elizondo[1], Marc Palà Sánchez[2], César Rodriguez- Emmenegger[3], Nina Yu. Kostina[4]

[1234]IBEC, Barcelona, España

Mucus at biointerfaces is often an insurmountable barrier to medicines and to any therapeutic interaction. In the airways, mucus protects the epithelium yet also shelters and supports the organization of bacteria. This is exacerbated in cystic fibrosis, where elevated calcium increases mucin cross-linking, raising mucus concentration and stiffness to the point that cilia collapse, promoting bacterial colonization and progressive tissue destruction. Synthetic cells are an emerging technology that learns from living organisms to perform functions that could be leveraged for medical purposes, but their size — above the micrometre range — prevents them from crossing such barriers. To circumvent this, we recently introduced ionic-combs, ionically-linked comb polymers that self-assemble into ionic-combisomes, a new class of polymer vesicles. Their membranes are exceptionally flexible, with a bending rigidity close to kT (1–15 kT). Placed on simulated mucus, ionicombisomes readily transport across it through two mechanisms: their high flexibility allows them to pass through tortuous open paths, and sacrificial polymers can be incorporated that bind to mucins and release calcium, breaking cross-links to open additional paths through which the deformable vesicles squeeze and reach the bottom of the barrier. In mucus from cystic fibrosis patients and in bronchial aspirates, ionicombisomes were capable of transporting across the barrier and reaching the bacteria beneath. These results introduce a concept for the transport of large objects across mucosal barriers and pave the way for applications in drug delivery, synthetic cells, and microbiome engineering.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 38 presented by:

NAME: Sergi Tosal

PolyQ expansion remodels the sequence and structural determinants of huntingtin nucleation

Sergi Tosal Castaño[1], Benedetta Bolognesi[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

Polyglutamine (polyQ) expansion in huntingtin (HTT) exon 1 is a central determinant of Huntington's disease-associated aggregation. Although the N-terminal 17-residue region (N17) and the C-terminal proline-rich domain (PRD) strongly modulate polyQ aggregation, how their contributions change with polyQ length remains unclear. Here, we used deep mutational scanning to systematically define the sequence determinants of HTT nucleation across polyQ lengths ranging from 25Q to 45Q, in the presence or absence of the first 11 prolines of the PRD.

We generated comprehensive single-amino-acid substitution libraries spanning N17 and quantified amyloid nucleation using a yeast Sup35-based selection assay. Across polyQ lengths, most N17 substitutions reduced nucleation, confirming the importance of an intact N17 region. However, the effects of individual substitutions were strongly dependent on polyQ length. A major transition emerged around 27Q, above which hydrophobic substitutions increasingly promoted nucleation, whereas glycine and proline substitutions became progressively inhibitory. Removal of polyP enhanced nucleation at shorter polyQ lengths, but this effect diminished with polyQ expansion, with mutation effects in the polyP and ΔP backgrounds converging from 33Q onward.

To investigate the structural basis of these changes, we examined N17 helicity and performed a second deep mutational scan of the terminal N17 tetrapeptide. PolyQ expansion selectively favored hydrophobic and α-helix-promoting motifs at the N17–polyQ interface. Consistent with this, nucleation correlated negatively with N17 helicity at 25Q but strongly positively at 45Q. Structural modelling further indicated that expansion-favored motifs stabilize N17 oligomers.

Together, our results reveal a polyQ-length-dependent switch in the mechanism of HTT nucleation. Short polyQ tracts are governed primarily by local sequence and conformational effects, whereas expanded polyQ increasingly favors hydrophobic, helical N17 motifs and N17 oligomerization. These findings provide a mechanistic framework for understanding how polyQ expansion remodels the molecular determinants of HTT aggregation.

POSTER 39 presented by:

NAME: Tomás Quiroga

The folding, dimerization and allosteric landscapes of the ALS protein SOD1: a comprehensive mutational atlas

Tomás Quiroga[1], Laz Ashcroft[2], Lauren Rice[2], Defne Boratav[3], Mariano Martín[1], Juan Francisco Vázquez-Costa[4], Bryony A Thompson[5], Luke McAlary[2], Benedetta Bolognesi[1]**

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology, Barcelona 08028, Spain.
[2] Molecular Horizons and School of Science, Faculty of Science, Medicine and Health, University of Wollongong, Wollongong, New South Wales, Australia, 2522.
[3] Department of Pediatrics, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Victoria, Australia, 3010.
[4] ALS Unit, Neurology Department, Hospital la Fe, IIS La Fe, CIBERER, University of Valencia, Valencia, Spain.
[5] Department of Pathology, The Royal Melbourne Hospital, Melbourne, Victoria, Australia, 3050.

Mutations in superoxide dismutase 1 (SOD1) can disturb monomer folding and dimerization, ultimately leading to the development of amyotrophic lateral sclerosis (ALS). Genotype-phenotype knowledge of SOD1 monomer folding and dimerization is largely incomplete, impeding our ability to treat and understand SOD1-ALS. To address this issue, we performed multidimensional deep mutational scanning of ~6,000 SOD1 variants (amino acid substitutions, insertions and deletions), quantifying folded monomer abundance, and measuring wild-type-variant heterodimerization. Importantly, both abundance and heterodimerization capture pathogenicity, with heterodimerization being a slightly better classifier of pathogenic variants. Notably, ~80% of pathogenic variants and ~70% of variants of uncertain significance in SOD1 perturb both monomer abundance and heterodimerization, pointing to protein destabilization as a major driver of SOD1-ALS. Orthogonal validation in mammalian cells shows that protein abundance strongly correlates with other disease-relevant phenotypes, including protein aggregation and toxicity. Although monomer abundance and heterodimerization are strongly coupled, residual effects identify variants that perturb the heterodimer beyond their impact on monomer folding. Mapping residual effects uncovers potential allosteric sites that modulate dimer stability independently of monomer folding, revealing mechanistic insights and potential therapeutic entry points to stabilize SOD1 as a dimer. Together, these results demonstrate that multidimensional phenotype variant mapping improves mechanistic understanding of SOD1 variants and clinical variant interpretation, while uncovering structural targets for SOD1-ALS treatment.

POSTER | ADVANCED THERAPEUTIC SYSTEMS

POSTER 40 presented by:

NAME: Yaiza Andrés

Deep Mutational Scanning of Tau Amyloid Nucleation

Yaiza Andrés Jeske[1], Mariano Martín[1], Benedetta Bolognesi[1]

[1] Institute for Bioengineering of Catalonia, Barcelona, Spain

The assembly of tau into amyloid filaments is associated with more than 20 neurodegenerative diseases, collectively termed tauopathies. Despite the importance of tau aggregation in disease, how sequence variation across tau influences amyloid nucleation remains poorly understood. Here, we use Deep Mutational Scanning to systematically quantify the effects of amino acid substitutions across the 2R, 3R and 4R regions of tau on amyloid nucleation. This approach allows us to map the mutational landscape of tau and capture key amyloidogenic regions, including the PHF6 and PHF6* motif. We are also investigating phosphomimetic mutations to determine how phosphorylation alters tau nucleation, and developing approaches to purify the tau fibrils formed in yeast for further characterisation. Together, these experiments aim to reveal the sequence and molecular determinants governing tau amyloid formation.

POSTER 41 presented by:

NAME: Yasaman Keshmiri

Tandem Enzymatic Activity of Catalase- and Glucose Oxidase- powered Nanomotors for Oxygen Generation and Therapeutic Modulation in Inflammatory Bowel Disease

Yasaman Sadat Keshmiri[1], José Raul Herance[2,3], Samuel Sánchez Ordoñez[1,4]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Baldiri i Reixac 10-12, 08028 Barcelona, Spain

[2] Medical Molecular Imaging Research Group, Vall d'Hebron Research Institute (VHIR), Nuclear Medicine, Radiology and Cardiology Departments, Vall d'Hebron University Hospital, Autonomous University Barcelona, Barcelona 08035, Spain

[3] CIBERBBN (Instituto de Salud Carlos III), Madrid 28029, Spain

[4] Institució Catalana de Recerca I Estudis Avancats (ICREA), 08010 Barcelona, Spain

Inflammatory bowel disease (IBD) is a chronic, relapsing disorder characterised by intestinal inflammation, epithelial barrier disruption, excessive reactive oxygen species production, and local tissue hypoxia [1,2]. Enzyme-powered nanomotors have emerged as active systems that convert biochemical substrates into motion while performing localised catalytic functions [3,4]. In this study, we develop two complementary populations of biodegradable poly(lactic-co-glycolic acid) (PLGA) nanomotors: catalase (CAT)-and glucose oxidase (GOx)-functionalised nanomotors. These formulations are optimised independently and will subsequently be evaluated together to establish tandem enzymatic activity. GOx catalyses glucose oxidation, producing gluconic acid and hydrogen peroxide (H_2O_2), whereas CAT decomposes H_2O_2 into water and oxygen. Combining the two nanomotor populations is intended to couple GOx-mediated H_2O_2 production with CAT-mediated H_2O_2 removal and local oxygen generation. PLGA nanoparticles are covalently functionalised with either CAT or GOx via EDC/NHS coupling. Different EDC/NHS and enzyme concentrations are evaluated to optimise functionalisation of each formulation. Particle size, polydispersity, and surface charge are analysed by dynamic light scattering (DLS) after nanoparticle synthesis and throughout the functionalisation process, while morphology is assessed by electron microscopy. Immobilised enzyme is quantified using the bicinchoninic acid (BCA) assay. Retained CAT activity is determined spectrophotometrically by monitoring H_2O_2 decomposition, whereas GOx activity is evaluated using an ABTS/horseradish peroxidase- coupled assay. Preliminary optimisation enabled the selection of separate CAT- and GOx- functionalised PLGA nanomotor formulations with suitable physicochemical properties, enzyme immobilisation, and retained catalytic function. Motion studies compare CAT nanomotors in the presence and absence of H_2O_2 and GOx nanomotors in the presence and absence of glucose. The optimised formulations will subsequently be combined to investigate tandem catalytic activity, oxygen generation, and motion under substrate concentrations and physicochemical conditions relevant to the intestinal environment. This work establishes the initial basis for a biodegradable, enzyme-powered nanomotor strategy to modulate the oxidative and hypoxic features of the IBD microenvironment.

References

1. Baumgart, D. C., & Sandborn, W. J. (2007). Gastroenterology 2 Infl ammatory bowel disease: clinical aspects and established and evolving therapies. In *www.thelancet.com* (Vol. 369). www.thelancet.com

2. Yang, X., Guo, H., & Zou, M. (2026). Inflammatory bowel diseases: pathological mechanisms and therapeutic perspectives. In *Molecular Biomedicine* (Vol. 7, Number 1). Springer Nature. https://doi.org/10.1186/s43556-025-00395-z

3. Ruiz-González, N., Esporrín-Ubieto, D., Kim, I. D., Wang, J., & Sánchez, S. (2025). Micro- and Nanomotors: Engineered Tools for Targeted and Efficient Biomedicine. In *ACS Nano* (Vol. 19, Number 9, pp. 8411–8432). American Chemical Society.

https://doi.org/10.1021/acsnano.4c12726

4. Credi, A. (2014). Nanomachines. Fundamentals and Applications. By Joseph Wang.

Angewandte Chemie International Edition, *53*(17), 4274–4275.

https://doi.org/10.1002/anie.201311274

FLASH PRESENTATION | BIOMODELS AND TISSUE ENGINEERING

FLASH 42 presented by:

NAME: Joel Àlvarez Puig

Modelling biomaterial-associated biofilm infections in *Galleria mellonella* for antibiotic susceptibility screening

Joel Àlvarez-Puig[1,2], Eduard Torrents[1,2]

[1] Bacterial infections and antimicrobial therapies group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Baldiri Reixac 15-21, 08028 Barcelona, Spain.

[2] Microbiology Section, Department of Genetics, Microbiology and Statistics, Faculty of Biology, Universitat de Barcelona, 643 Diagonal Ave., 08028, Barcelona, Spain.

Biomaterial-associated infections pose a major challenge due to biofilm formation and the resulting changes in antibiotic susceptibility. Current in vitro models cannot fully and accurately reproduce infections in living organisms. While studies using mammalian models offer greater biological relevance, they are often very costly and ethically constrained. In this study, we establish a *Galleria mellonella* model to study colonization, infection and treatment of biofilm-associated infections caused by various pathogens on titanium and silicone surfaces. This approach allows a rapid, cost-effective screening method within an in vivo immune context, offering a versatile platform for identifying more effective therapeutic strategies.

Acknowledgements

This work was partially supported by grants PID2024-158622OB-I00, PID2021-125801OB-100, PLEC2022-009356 and PDC2022-133577-I00 funded by MCIN/AEI/ 10.13039/501100011033 and "ERDF A way of making Europe", the CERCA programme and *AGAUR-Generalitat de Catalunya* (European Regional Development Fund FEDER) (2021SGR-00092 and 2021SGR01545) and Catalan Cystic Fibrosis association. E.T. is a researcher of the ICREA Academia 2025 program. J.A. thanks Ministerio de Ciencia, Innovación y Universidades for its financial support through the FPI program (PRE2022-102478).

FLASH 43 presented by:

NAME: David Bartolomé Català

Microphysiological reconstruction of the colonic tumor microenvironment for T cell migration studies

David Bartolomé-Català [1], Pau Canaleta Vicente [1], Jordi Comelles [2,3], María García- Díaz[2,3], Elena Martínez [1, 2, 3,4]

[1] Biomimetic Systems for Cell Engineering Laboratory, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain

[2] Department of Electronics and Biomedical Engineering, University of Barcelona (UB), Barcelona, Spain

[3] Fraunhofer Center for Applied Theragnostics (Fraunhofer CAT), Barcelona, Spain

[4] Centro de Investigación Biomédica en Red (CIBER), Barcelona, Spain

The immune system plays a pivotal role in cancer progression and response to therapy, with T cells acting as central mediators of anti-tumor immunity. Effective tumor infiltration by T cells requires a coordinated, multistep process involving transendothelial migration, navigation through the stroma, and subsequent access to the epithelial tumor region. However, the mechanisms governing T cell migration within the tumor microenvironment remain poorly understood. The inherent complexity and limited accessibility of in vivo systems make these processes challenging to study, driving the development of microphysiological systems that more faithfully recapitulate tissue architecture and cellular heterogeneity. In this context, the use of primary cells is particularly important, as it preserves the physiological heterogeneity and authenticity of native tissues, enabling experimental outcomes that more closely reflect in vivo conditions. Here, we present a three-dimensional in vitro approach to investigate T lymphocyte migration in colorectal cancer. Using organ-on-a-chip technology, we developed a microphysiological system composed of three interconnected microchannels. The epithelial compartment was lined with a three-dimensional tubular monolayer derived from healthy or tumor mouse colon organoids. The central stromal compartment contained primary intestinal fibroblasts embedded in a collagen-Matrigel hydrogel, while an endothelial compartment formed by MS1 endothelial cells served as the entry point for primary T lymphocytes. This spatially organized architecture recapitulates key structural features of the colonic wall and enables the investigation of T cell migration along the critical endothelium–stroma– epithelium axis. Notably, our results revealed greater T lymphocyte infiltration in the tumor-derived epithelial compartment compared with healthy epithelium, highlighting differences in immune cell recruitment and trafficking between healthy and tumor tissues. This platform therefore provides a physiologically relevant model to dissect the cellular and microenvironmental mechanisms underlying T cell infiltration in colorectal cancer and may serve as a valuable tool for studying anti-tumor immune responses and therapeutic strategies.

FLASH 44 presented by:

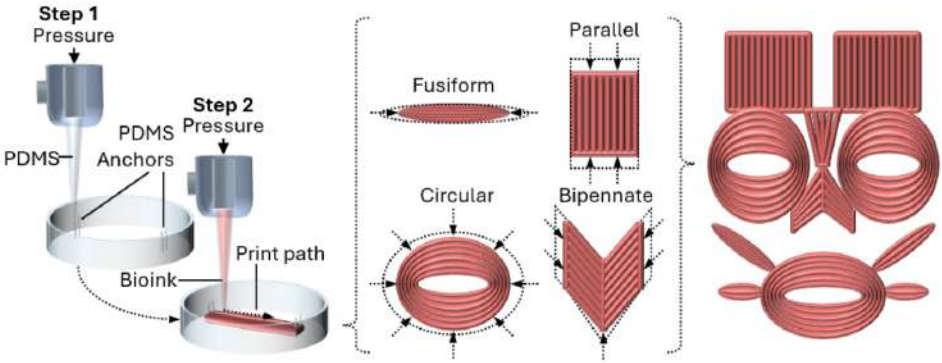
NAME: Florencia Lezcano

Toward biohybrid facial actuation: 3D bioprinting of functional skeletal muscle systems

Florencia Lezcano[1], Marina Rovira[1], Judith Fuentes[1], Serxio Álvarez[1], Samuel Sánchez[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.

To reproduce the complexity of human facial expression with bioengineered skeletal muscle, it is essential to replicate the native tissue architecture. This study presents a functional system composed of multiple 3D-bioprinted skeletal muscle constructs replicating the morphology and myofiber architecture of facial musculature. Constructs representing the main superficial facial muscles were fabricated using an extrusionbased bioprinter and cultured under mechanical stress to guide myofiber orientation. After 14 days in culture, constructs exhibited mature myotubes and biomimetic myofiber architecture. Under electrical stimulation, constructs reproduced native contractile function both individually and as an integrated system. This approach advances bioengineered skeletal muscle systems for next-generation biohybrid robotics.



FLASH 45 presented by:

NAME: Andreu Matamoros Anglès

Extracellular vesicles in Alzheimer's disease: Amyloid β aggregation and neuronal network dysfunction

A. Matamoros-Angles[1,2], M. Shafiq[1], T. Börtsler[3], L. Pérez[4], M. Riu-Villanueva[5], O.A.A. Mohamed[1], L. Amin[6], S. C. Meister[1], E. Karadjuzovic[1], S. Da Vela[7], B. Mohammadi[1], L. Ordóñez-Gutiérrez[8], A. Correia[9], M. Schmitz[9], B. Siebels[10], H. Schlüter[10], I. Ferrer[11], S. Krasemann[1], F. Wandosell[8], I. Zerr[9], H. C. Altmeppen[1], M. Schweizer[12], M. Woo[13], B. Winner[3], D. Svergun[7], D. A. Harris[6], C. Seuring[14], F. Zunke[15], J. Soriano[4,5], J. A. Del Río[5], M. Glatzel[1]

[1] *Institute of Neuropathology, University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany.*
[2] *Faculty of Medicine, University of Vic-Central University of Catalonia, Vic, Catalonia, Spain. / Institut de Recerca I Innovació en Ciències de La Vida I de La Salut a La Catalunya Central (IrisCC), Vic, Catalonia, Spain.*
[3] *Department of Stem Cell Biology, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg (FAU), Erlangen, Germany. Center for Rare Diseases Erlangen (ZSEER), University Hospital Erlangen, FAU Erlangen-Nürnberg, Erlangen, Germany.*
[4] *Departament de Física de la Matèria Condensada, Universitat de Barcelona, Barcelona, Spain. / Universitat de Barcelona Institute of Complex Systems (UBICS), Barcelona, Spain.*
[5] *Molecular and Cellular Neurobiotechnology, Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Science Park of Barcelona, Barcelona / Department of Cell Biology, Physiology and Immunology, Faculty of Biology, University of Barcelona, Barcelona, Spain / Network Center for Biomedical Research of Neurodegenerative Diseases (CIBERNED), Institute Carlos III, Ministry of Health, Barcelona, Spain / Institute of Neuroscience, University of Barcelona, Barcelona, Spain*
[6] *Department of Biochemistry, Boston University School of Medicine, Boston, MA, USA*
[7] *European Molecular Biology Laboratory (EMBL), Hamburg, Germany*
[8] *Centro de Biología Molecular "Severo Ochoa" (CSIC-UAM), Universidad Autónoma de Madrid, Madrid, Spain*
[9] *Department of Neurology, University Medical Center Goettingen (UMG), Goettingen, Germany*
[10] *Institute of Clinical Chemistry and Laboratory Medicine, University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany*
[11] *Bellvitge University Hospital, IDIBELL, L'Hospitalet de Llobregat, Spain*
[12] *Core Facility Morphology & Electron Microscopy, ZMNH, University Medical Center Hamburg-Eppendorf, 20251 Hamburg, Germany.*
[13] *Translational Neurodegeneration Laboratory, Department of Neurology, University Medical Center HamburgEppendorf, Hamburg, Germany / Translational Neuroimaging Laboratory, The McGill University Research Centre for Studies in Aging, Montreal Neurological Institute, Montreal, Canada / Institute of Neuroimmunology and Multiple Sclerosis, University Medical Center Hamburg-Eppendorf, Hamburg, Germany*
[14] *Multi-User CryoEM facility, Centre for Structural Systems Biology (CSSB), Hamburg, Germany*
[15] *Department of Molecular Neurology, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Erlangen, Germany*

Extracellular vesicles (EVs) are nanosized lipid vesicles released by all cell types that participate in cell-to-cell communication, both within and outside their tissue of origin, which carry bioactive cargo, including RNA (e.g., mRNA, microRNA), enzymes, and surface protein receptors. Recently, EVs have emerged as potential mediators of pathology in sporadic Alzheimer's disease (sAD), putatively participating in the seeding and spreading of the pathological protein aggregates (i.e. Aβ amyloid plaques and p-Tau tangles). However, it is not yet known how EVs mechanistically exert this role, and, specifically, which molecules drive their function. In this context, we postulate that cellular prion protein (PrP^C), a GPI-anchored protein widely present on EVs, may explain EVs' role in sAD, as it has been described as a neuronal Aβ receptor.

This study aims to elucidate the molecular, structural, and functional roles of EVs in sAD pathophysiology, focusing on Aβ aggregation and neuronal network regulation.

We combined *in vitro* neuronal models, structural biology approaches, and analyses of human and mouse brain-derived EVs (BDEVs) to define the contribution of EV-associated PrP^C in Aβ amyloid plaque formation. PrP^C-expressing/deficient EVs from Neuro-2a cells and mouse brain tissue were incubated with recombinant Aβ and analysed using small-angle X-ray scattering, super-resolution microscopy, and cryogenic electron tomography. We characterised BDEVs from sAD and control frontal cortex autopsies using nanoparticle tracking analysis, electron microscopy, western blotting, and omics. Human iPSC-derived cortical neurons from healthy donors were treated to assess sAD-EV-mediated functional effects.

PrP^C-expressing EVs showed enhanced Aβ sequestration and fibrillation compared to PrP-deficient EVs, and PrP^C levels positively correlated with Aβ abundance in human sAD-BDEVs. EV markers, particularly those associated with PrP^C-positive EVs, were enriched within Aβ plaques in human tissue and amyloid mouse models. Omic profiling revealed that sAD-derived BDEVs differentially express metabolic enzymes, vesicle trafficking proteins, and synaptic proteins compared with control BDEVs. Neuron network activity analysis using calcium imaging in hiPSC-derived cortical neurons treated with BDEVs (from sAD or Ctrl patients) demonstrated that these EV-associated proteins modulate neuronal activity, reducing network clustering and inducing network perturbations and epileptic-like features. Finally, omics analysis of the treated hiPSC-derived neurons shows alterations in relevant biological functions (e.g., axon guidance, ribosome activity, energy metabolism) that explain the underlying molecular mechanisms of their effects in recipient neurons.

These findings indicate that EV-associated PrP^C participates in Aβ amyloid formation and that disease-specific EV cargo contributes to neuronal activity dysfunction, highlighting EVs as mechanistic drivers in sAD pathophysiology. These results provide a solid foundation for further studies on the detailed molecular mechanisms underlying the EV role in sAD, especially their effects on inhibitory neurons.

FLASH 46 presented by:

NAME: Nicolle Miranda de Lima

Engineering a Scalable and Highly Sensitive Microfluidic Platform for Real-Time Hyperpolarised ^{13}C Metabolic Imaging of 3D Hepatoblastoma Models

Nicolle Lima[1], María Alejandra Ortega Machuca[1]*, Vicente Ribas[1], Gergo Matajsz[1], Nichlas Vous Christensen[2], Lotte Bonde Bertelsen[2], Juan D. Sanchez-Heredia[3], Irene Marco Rius[1]*

[1] The Institute for Bioengineering IBEC, Barcelona, Spain

[2] The MR Research Centre, Aarhus University, Aarhus, Denmark

[3] JD Coils, Hamburg, Germany

Hyperpolarised magnetic resonance enables real-time investigation of cellular metabolism with greatly enhanced sensitivity [1]. However, its application to cell-based models remains technically challenging due to the short lifetime of the hyperpolarised signal, reproducible substrate delivery, and simultaneous analysis of multiple biological samples. These challenges are particularly relevant for rare diseases such as hepatoblastoma, where access to patient-derived biological material is often limited.

Our group previously developed a cell-based microfluidic platform, integrating 3D in vitro models with hyperpolarised magnetic resonance spectroscopic imaging (HP-MRSI) for parallel and longitudinal metabolic analysis [2,3]. However, detection sensitivity remains a limitation. Here, we present a new modular microfluidic system designed for integration with individual RF microcoils developed by our collaborators at Aarhus University [4], aiming to improve detection sensitivity while maintaining compatibility with preclinical and clinical MRI scanners.

The current prototype consists of a three-chamber PDMS chip for hepatoblastoma cells cultured in highly porous carboxymethylcellulose-based (CMC) scaffolds, with each 6 mm chamber aligned with an individual RF microcoil. The chip comprises two functional layers: one enabling continuous recirculation of cell culture medium and another providing rapid and controlled injection of the hyperpolarised substrate.

Computational fluid dynamics simulations are being performed to optimise the chip geometry and flow conditions prior to fabrication. Different designs and operating conditions are being evaluated based on velocity and pressure distributions, residence times, and substrate transport, with particular emphasis on homogeneous and reproducible delivery across the three chambers. The optimised design will be fabricated and experimentally characterised, including fluid delivery and chamber filling dynamics.

The three-chamber prototype will provide the basis for scaling the modular design to ten chips, yielding 30 independent culture chambers, and integrating a 30-channel microcoil detection system based on the previously reported high-throughput approach [4]. This strategy aims to enable real-time hyperpolarised ^{13}C metabolic analysis with improved sensitivity and reduced cellular requirements, providing a scalable platform for hepatoblastoma and other rare disease models.

References

[1] Marco-Rius, I. et al. (2026). *Disease Models & Mechanisms*, 19. DOI: 10.1242/dmm.052817

[2] Gomez-Cabeza, D. et al. (2026). *bioRxiv*. DOI: 10.64898/2026.07.16.738913

[3] Yeste, J. et al. (2023). *Lab on a Chip*, 23, 4950–4958. DOI: 10.1039/d3lc00474k

[4] Christensen, N. V. et al. (2025). *NMR in Biomedicine*, 38, e70174. DOI: 10.1002/nbm.70174

FLASH PRESENTATION | BIOMODELS AND TISSUE ENGINEERING

FLASH 47 presented by:

NAME: Chiara Ninfali

A Human 3D Platform combining Engineered Skeletal Muscle and Pancreatic Cancer Spheroids to model Cancer-Associated Cachexia

Chiara Ninfali[1,2], Marc Beltrà[2,3], Marta Fornaro[4], Javier Ramón-Azcon[1,2,5], Juan M. Fernández Costa[1,2]

[1] *Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain*
[2] *The Barcelona Institute of Science and Technology (BIST), Spain*
[3] *Institute for Research in Biomedicine (IRB Barcelona), Spain*
[4] *Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy*
[5] *ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain*

Cancer-associated cachexia (CAC) is a systemic syndrome characterized by progressive skeletal muscle wasting and metabolic dysfunction, affecting many patients with advanced cancer and contributing to poor treatment tolerance and survival. Despite its clinical impact, no approved therapies are available. Research on cancer-induced muscle wasting relies largely on in vivo animal models and, for mechanistic studies and drug screening, on conventional 2D myotube cultures exposed to tumor-derived conditioned media. While animal models provide valuable insights into systemic mechanisms, they are costly and have limited translation to human disease. Conversely, 2D models poorly reproduce the architecture, maturation, extracellular matrix, and functional properties of human skeletal muscle. Within the framework of the MOCAChip project (BIST Ignite 8th edition), we developed a human 3D in vitro model to investigate skeletal muscle responses to cachectic stimuli. A 3D pancreatic cancer model was generated using pancreatic cancer cell-derived spheroids embedded in collagen hydrogels. In parallel, engineered skeletal muscle tissues were generated from patientderived human myoblasts embedded in a fibrin–Matrigel matrix and cultured in 3D-printed chambers with two flexible pillars, promoting aligned and functional myofibers. Male- and female-derived myoblasts were included to investigate sex-dependent responses, which remain poorly characterized in CAC. The engineered tissues developed functional contractile properties that could be quantitatively assessed by electrical stimulation. Exposure to conditioned medium from pancreatic cancer spheroids reduced muscle contractile force, with a more pronounced effect in male-derived tissues in this experimental setting. This impairment was accompanied by reduced myotube cross-sectional area, consistent with an atrophic phenotype. RNA sequencing revealed alterations in metabolic pathways, including those related to mitochondrial metabolism. Consistently, respirometry analysis of male-derived tissues showed a modest reduction in mitochondrial respiratory capacity following exposure to cancer-derived conditioned medium. These results establish a human 3D platform with functional readouts to investigate early skeletal muscle responses to cancer-associated cachectic stimuli under controlled conditions. The model integrates functional, morphological, transcriptomic, and metabolic analyses and provides a foundation for investigating sex-dependent responses and inter-organ crosstalk in cancer cachexia, as well as for future therapeutic screening.

FLASH 48 presented by:
NAME: Anna Panteleeva

Monitoring Neurodegeneration in a Brain-on-a-Chip with an NfL Biosensor

A. Panteleeva[1,3], S. Palma-Florez[1,3], J. Samitier[1,2,3], M. Mir[2,1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.
[2] Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), Madrid, Spain.
[3] University of Barcelona (UB), Barcelona, Spain.

Alzheimer's disease and other neurodegenerative diseases (NDDs) are a serious challenge for our aging society [1]. Although we now have a better understanding of how NDDs develop and what causes them, finding effective treatments remains difficult, as many promising candidates fail in clinical trials [2,3]. One reason is that current in vitro models often rely on endpoint measurements, making it difficult to follow how neuronal damage develops over time.

We are developing a brain-on-a-chip (BoC) system that can monitor neurodegeneration as it happens. The system includes an electrochemical biosensor for neurofilament light (NfL), a protein released following axonal damage [4], allowing NfL levels to be followed over time. The chip also recreates key features of the blood-brain barrier (BBB) by co-culturing endothelial cells, pericytes, astrocytes, and neurons (differentiated from long-term human neuroepithelial-like stem cells) under continuous perfusion. Integrated transepithelial/transendothelial electrical resistance (TEER) sensors are used to monitor BBB integrity alongside NfL release.

The NfL biosensor was first characterised outside the chip, reaching limits of detection of approximately 3 pg mL^{-1} in PBS and 9 pg mL^{-1} in cell culture medium. In PBS, the working range extended from 10 to $\geq 5 \times 10^7$ pg mL^{-1}. NfL detection was also demonstrated in media collected from cultured neurons.

By integrating the biosensor into the brain-on-a-chip, we aim to move from single endpoint measurements towards continuous monitoring of neuronal damage and BBB function, providing a more dynamic way to study neurodegeneration and test potential treatments.

1. Feigin, V.L. et al., *Lancet Neurol.* **2020**, *19*, 255.
2. Kim, C.K. et al., *Journal of Alzheimer's Disease* **2022**, *87*, 83–100.
3. Cummings, J. et al., *Alzheimers Dement (N Y)* **2019**, *5*, 272–293.
4. Hansson, O. et al., *Neurology* **2017**, *88*.

FLASH 49 presented by:

NAME: Francisco Manuel Sáez González

From Organoids to Assembloids: Modeling Neurovascular Dynamics in Spinal Cord Injury

Francisco M. Sáez[1], Carla Batlle[1], Giacomo Ena[1], Eloi Montañez[3,4], J. Alberto Ortega[2,3], Zaida Álvarez[1,5,6]

[1] Biomaterials for Neural Regeneration Group, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

[2] Department of Pathology and Experimental Therapeutics, Institute of Neurosciences, University of Barcelona, L'Hospitalet del Llobregat, Barcelona, Spain

[3] Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), L'Hospitalet del Llobregat, Spain

[4] Department of Physiological Sciences, Faculty of Medicine and Health Sciences, University of Barcelona, L'Hospitalet del Llobregat, Spain

[5] CIBER en Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Madrid, Spain

[6] Center for Regenerative Nanomedicine (CRN), Northwestern University, 303 E. Superior St, 60611, Chicago, USA

Stem cell–derived three-dimensional neural models are increasingly used to investigate human tissue development and neurological disorders. Yet the limited physiological complexity and *in vivo* microenvironment recapitulation of current systems - particularly the absence of vascular and multicellular interactions - continues to constrain their ability to faithfully model human pathology. This study establishes a humanized spinal cord injury (SCI) model through the integration of human neural and vascular organoids as physiological relevant systems for injury research and treatment validation.

Human spinal cord and vascular organoids (hSCOs and hVOs) were derived from hiPSCs through stepwise exposure to patterning small molecules directing neuroectodermal and mesodermal lineage specification. Organoids were subsequently fused at defined developmental stages to generate vascularized spinal cord organoids (hVSCOs). To model SCI *in vitro*, hVSCOs were subjected to a controlled mechanical impact using the Infinite Horizon Impactor system. Neurovascular architecture, neural electrophysiological activity, and molecular responses to injury were assessed by immunohistochemistry, multielectrode array (MEA) recordings, quantitative proteomics, and bulk RNA sequencing.

Following contusive injury, hVSCOs reproduced key pathological hallmarks of human SCI, including astrocyte-driven glial scar formation, increased caspase-3–associated apoptosis, expansion of $Ki67^+$ progenitor populations, disruption of vascular and neural architecture, $IBA1^+$ microglial activation, and a marked reduction in electrophysiological activity by MEA recordings. Proteomic profiling further revealed that vascularization distinctly shapes the molecular response to injury, with hVSCOs displaying differential protein expression patterns compared to non-vascularized controls under both homeostatic and injured conditions.

Together, these findings establish hVSCOs as a physiologically relevant, humanized platform that captures key neurovascular features of SCI, offering a valuable tool for translational research and preclinical evaluation of regenerative therapies.

Acknowledgments

The project leading to these results has received funding from" la Caixa" Foundation under the project code LCF/PR/HR25/52450044, and NIH NIA R01AG086270. The content solely reflects the author's views.

FLASH 50 presented by:

NAME: Jarmila Stankova

Spatially resolved analysis of CRISPR-mediated metabolic gene knockouts in tumor xenografts

Jarmila Stankova[1], Michela Lain Contato[1], Sergi Casellas Diaz[1], Xavier Rovira Clave[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

Tumor metabolism and its regulatory networks play a central role in shaping cancer progression and the tumor microenvironment. However, how co-existing cell-intrinsic metabolic alterations interact and spatially distribute within the tumor microenvironment remains unclear. We combined CRISPR-based gene perturbation with bulk RNA sequencing and spatially resolved omics to investigate how metabolic gene knockouts (KO) influence tumor growth and tissue organization *in vivo*.

We generated HCT116 colorectal cancer KO lines targeting *STK11* (AMPK upstream regulatory kinase), *SLC16A1* (monocarboxylate transporter), *MTR* (methionine synthase), and *ACSL4* (long-chain fatty acid metabolism). Each KO line was uniquely barcoded using protein epitope tags for multiplexed tracking. Gene editing efficiency was validated using ICE analysis for all targets, with additional confirmation of *ACSL4* knockout by Western blot, showing concordance between gene disruption and protein expression. Bulk RNA sequencing across all KO lines revealed distinct compensation signatures. Pathway-level analysis identified proliferation and pyrimidine synthesis gene sets as the most variable across conditions.

KO cells were pooled into two groups: Pool 1 (*STK11* KO plus barcoded WT cells) and Pool 2 (*SLC16A1*, *MTR*, *ACSL4* KOs plus barcoded WT cells) and injected into NSG mouse xenograft models. FFPE sections were analyzed using Imaging Mass Cytometry (IMC), enabling spatial debarcoding and mapping of KO-specific cell populations within the tumor architecture. All FFPE samples were characterized by H&E staining, and Pool 2 tumors were further analyzed by immunohistochemistry for immune and stromal markers (Ly6G, F4/80, vimentin, and αSMA).

Initial analyses reveal spatially localized distributions of KO populations and demonstrate the ability to link genetic perturbations with local metabolic and microenvironmental features. Both KO pools showed extensive necrosis. In pool 2, MTR KO cells predominated, consistent with their low stress-response transcriptional signature and metabolic self-sufficiency. Ongoing work focuses on quantifying spatial growth dynamics and defining how specific metabolic perturbations shape tumor composition, immune infiltration, and stromal interactions. This integrated approach establishes a scalable framework for studying metabolic dependencies in cancer within their native spatial context.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 51 presented by:

NAME: Agnieszka Nikitiuk

Beyond The Cell: Engineering The HPV-Negative HNSCC Microenvironment for Matrix-Dependent Drug Screening

A. Nikitiuk[1], J. Lopez Avila[1,2], P. Ucla[3], O. Castaño[1,2,4], E. Engel[1,4,5], N. M. Coelho[1]

[1] Biomaterials for Regenerative Therapies Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain

[2] University of Barcelona (UB), Barcelona, Spain

[3] Cellular and molecular mechanobiology, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain

[4] CIBER en Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Madrid, Spain

[5] IMEM-BRT Group, Department of Materials Science and Engineering, EEBE, Universitat Politècnica de Catalunya (UPC)

Head and neck squamous cell carcinoma (HNSCC) is a heterogenous malignancy in which tumor microenvironment (TME) influences tumor growth, invasion, and response to treatment. HPV-negative HNSCC is generally associated with more aggressive disease and poorer treatment outcomes than HPV-positive HNSCC, highlighting the need for preclinical models that capture its invasive and treatment-resistant phenotype. Building on a previously established HPV-stratified 3D HNSCC platform, this study focuses on the HPV-negative models and investigates how extracellular matrix composition affects tumor behavior and chemotherapy response.

Multicellular spheroids were generated from HPV-negative HNSCC cells and embedded in collagen, fibrin, or collagen enriched with cell-derived matrix (CDM). Selected models also included fibroblasts within the matrix to increase stromal complexity. Matrix properties were assessed using rheology and nanoindentation, while spheroid growth, invasion, and structural organization were evaluated by imaging and quantitative morphometric analysis. By the day 10, CDM-enriched collagen facilities cell invasion, reaching 3.5-fold increase, while rigid fibrin only 1.6-fold increase compared to the spheroid prior to transfer. Soft collagen (2 kPa) demonstrated the highest level of porosity, reaching 89.9±0.46 %, while thicker fibrin (2.8 kPa) showed the least porous structure (76.5±0.98 %). The response to doxorubicin was assessed by viability and dose-response assays. Matrix composition strongly influenced spheroids' morphology and behavior. Collagen enriched with CDM supported the greatest tumor cell invasion and matrix remodeling, whereas fibrin, which showed higher mechanical resistance, constrained spheroid expansion. The different matrices also produced distinct matrix remodeling, and drug transport. Doxorubicin response was matrix-dependent, with collagen-based condition showing higher IC_{50} values (IC_{50} = 1.25 µm, IC_{50} = 2.1 µm, for collagen-CDM and collagen, respectively) than the more restrictive fibrin condition (IC_{50} = 0.13 µm). Fibroblast-containing constructs showed increased matrix remodeling and reduced drug sensitivity compared with simpler tumor spheroids.

These findings demonstrate that the extracellular matrix is an important determinant of phenotype and chemotherapy response in 3D HPV-negative HNSCC models. Comparison of collagen, fibrin and CDM-enriched collagen provides a controlled strategy for studying how matrix composition and mechanics influence tumor invasion and chemoresistance. The platform may improve the biological relevance of preclinical HNSCC drug screening, although further validation with patient-derived samples and clinical response data will be required.

POSTER 52 presented by:

NAME: Ainoa Tejedera-Villafranca

Modeling Duchenne Muscular Dystrophy Cardiomyopathy Using hiPSC-Derived 3D Cardiac Co-Cultures

Ainoa Tejedera-Villafranca[1], Javier Ramón-Azcón[1,2], Juan M Fernández-Costa[1]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain

Duchenne muscular dystrophy (DMD) is a severe, progressive genetic disorder caused by the absence of protein dystrophin, leading to widespread and irreversible muscle degeneration. While skeletal muscle wasting is the most prominent clinical hallmark, progressive cardiomyopathy is ultimately the leading cause of mortality in these patients. However, the development of curative, anti-fibrotic treatments for DMD-associated cardiac damage is hindered by a lack of preclinical models that accurately replicate human cardiac tissue dynamics. As part of the multidisciplinary BEAT Consortium, our research at IBEC aims to bridge this gap by developing an advanced Heart-on-a-Chip (HoC) platform for disease modeling and drug screening.

Our current efforts are centered on establishing the biological and biomechanical foundation for this platform using human induced pluripotent stem cell (hiPSC) technologies. First, we are characterizing the baseline fibrotic phenotype of hiPSC-derived cardiac fibroblasts generated from DMD and healthy control lines. Concurrently, we are developing functional 3D engineered heart tissues (EHT) by co-culturing these fibroblasts with hiPSC-derived cardiomyocytes. By casting and anchoring these 3D constructs on a microfabricated post system, we drive structural alignment and cellular maturation. Crucially, this setup enables dynamic evaluation of tissue contractility and biomechanical deficits associated with DMD-induced fibrosis. Once fully adapted, these hiPSC-derived 3D cardiac co-cultures will form the biological core of a multiplexed organ-on-chip platform capable of real-time tissue injury monitoring. Ultimately, this bioengineered model will provide a robust preclinical tool for uncovering novel fibrotic mechanisms and evaluating the efficacy of next-generation, anti-fibrotic therapies for DMD cardiomyopathy.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 53 presented by:

NAME: Alba Calonge Sanz

Optimization of Calu-3 and primary bronchial epithelial cell (PBEC) air-liquid interface (ALI) models for investigating chronic *Pseudomonas aeruginosa* respiratory infections

Alba Calonge-Sanz[1,2], Joana Admella[1,2], Dennis K. Ninaber[3], Pieter S. Hiemstra[3], Anne M. van der Does[3] and Eduard Torrents[1,2]*.*

[1] Bacterial infections and antimicrobial therapies group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST). Baldiri Reixac 15-21. 08028 Barcelona, Spain.

[2] Microbiology Section, Department of Genetics, Microbiology and Statistics, Faculty of Biology, University of Barcelona, 643 Diagonal Ave., 08028, Barcelona, Spain.

[3] PulmoScience Lab, Department of Pulmonology, Leiden University Medical Center, Leiden, The Netherlands.

Pseudomonas aeruginosa is an opportunistic pathogen involved in chronic respiratory infections, especially concerning in bronchiectasis-related diseases such as cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD). Impaired mucociliary clearance and dehydrated mucus accumulation in these conditions create niches that favour bacterial persistence. In these infections, *P. aeruginosa* is often found in the form of biofilms, highly structured bacterial communities embedded in a self-produced extracellular polymeric substance (EPS), which show increased antimicrobial tolerance and enhanced immune evasion.

Air-liquid interface (ALI) cell models mimic the airway epithelium *in vitro*, but most existing systems, when co-cultured with *P. aeruginosa*, experience significant damage to the epithelial barrier soon after exposure due to the rapid secretion of bacterial virulence factors. This makes it difficult to develop an *in vitro* model that accurately reproduces long-term interactions between the infecting bacteria and the epithelial layer.

This project aims to develop a reliable and reproducible *P. aeruginosa* biofilm model that does not compromise cell viability, using the airway epithelial cell line Calu-3 and primary bronchial epithelial cells (PBECs) as a more physiologically relevant system. This model will enable the study of long-term host-pathogen interactions, biofilm development, antimicrobial resistance, and the role of mucus during disease progression, with the aim of providing deeper insights into these clinically relevant chronic infections.

This study was supported by grants PID2024-158933OB-I00 funded by MCIN/AEI/10.13039/501100011033 and “ERDF A way of making Europe”; the CERCA programme and AGAUR-Generalitat de Catalunya (grant number 2021SGR01545), by the European Regional Development Fund (FEDER) and the Catalan Cystic Fibrosis association. E.T. is a researcher of the ICREA Academia 2025 program. A.C.S is supported by a predoctoral fellowship funded by the Spanish State Research Agency (AEI) (Grant PREX2023-000036, funded by MICIU/AEI/10.13039/501100011033). This collaboration was supported by a FEMS Research and Training Grant awarded to A.C.S., which enabled her research stay at the Leiden University Medical Center.

POSTER 54 presented by:
NAME: Angela M. Ramírez Rosales

Nanocellulose & Bacterial Cellulose for Medical and Environmental Applications

Angela M. Ramírez Rosales[1,2], Javier Gómez Fernández[1,3]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain
[2] Department of Biomedicine, School of Medicine, University of Barcelona, Barcelona Spain
[3] Catalan Institute for Research and Advanced Studies (ICREA), Barcelona, Spain

Biomedical research needs to evolve towards more accurate, sustainable and human-relevant models. This transformation can be achieved by following the concept of Non-Animal Methods (NAMs) and integrating naturally-existing biomaterials. Cellulose polysaccharide material is the most abundant natural polymer on Earth. Bacterial nanocellulose (BNC) is biosynthesized primarily by certain species of acetic acid bacteria, such as *Komagataeibacter xylinus*, with high purity levels. Despite being biocompatible, cellulose is generally considered bioinert and has low cell-adhesive properties, which can limit its interaction with cells, but can be harnessed in tissue engineering to culture embryoid bodies. The project will focus on optimizing the production of Bacterial Nanocellulose and BNC derivates, and introducing the material into a Microphysiological to seed a culture of Embryoid Bodies (EBs), considering mechanical cues and stimulations, contributing to non-animal methods to study pluripotent stem cell differentiation and early human embryonic stages.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 55 presented by:

NAME: Anna Vilche Mariscal

Tuning Hydrogel Network Architecture in PEG–HA-Norbornene Hydrogels Enhances Brain Organoid Diffusion and Maturation

Anna Vilche[1,3], Valerie Katimi[5,6], Daniel Sierra[5,6], Joan Mañez[1], Susana Rodriguez[1], Elena Xuriguera[2], J. Alberto Ortega[5,6], Zaida Alvarez[1,7], Oscar Castaño[3,4,7,8]

[1] Biomaterials for Neural Regeneration Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.

[2] MaterialsScience and Physical Chemistry, University of Barcelona, Barcelona, Spain

[3] Electronics and biomedical engineering, University of Barcelona, Barcelona, Spain.

[4] Biomaterials for Regenerative Therapies, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona 08028, Spain·[5]Pathology and Experimental Therapeutics, Institute of Neurosciences, University of Barcelona, L'Hospitalet de Llobregat, Barcelona,Spain

[6] Institut d'Investigacio Biomèdica de Bellvitge (IDIBELL), L'Hospitalet del Llobregat, Spain [7]CIBER en Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Madrid, Spain.

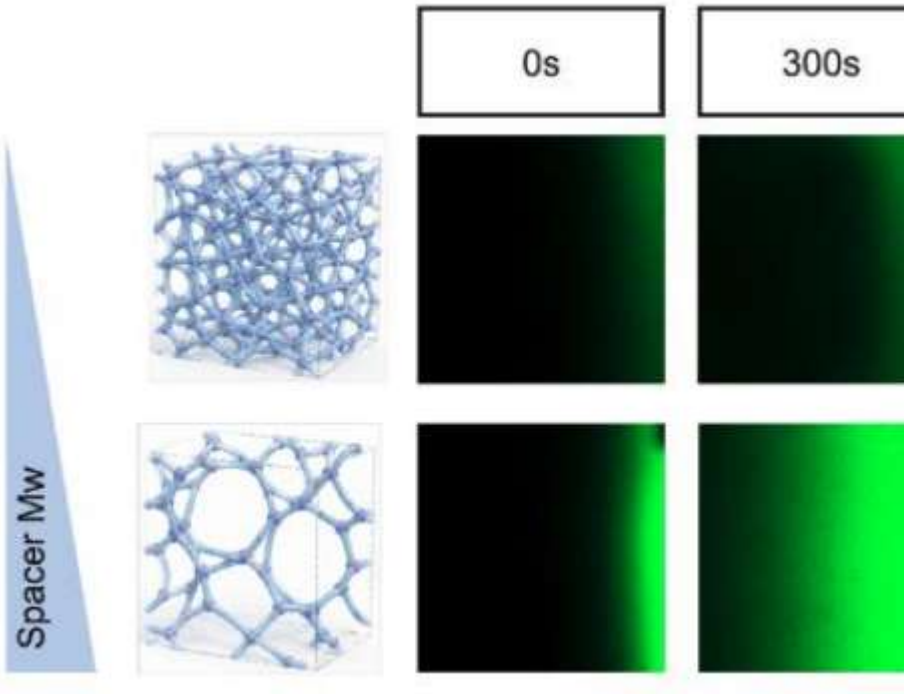
[8] Institute of Nanoscience and Nanotechnology (IN2UB), University of Barcelona (UB), Barcelona, Spain.

Brain organoid models require extracellular matrices that provide physiologically relevant mechanical properties while allowing sufficient molecular transport and cellular remodeling to support tissue growth and maturation. However, reproducing these features simultaneously remains challenging, as conventional hydrogel systems often couple matrix stiffness with polymer network density and mesh size. [1] [2] Here, we developed PEG-tuned hyaluronic acid (HA)-norbornene hydrogels based on thiol– ene photochemistry to independently modulate network architecture while maintaining mechanical properties within the range of central nervous system (CNS) tissue. HA was functionalized with norbornene groups and crosslinked with PEG-dithiol crosslinkers ranging from 2,000 to 5,000 Da to tune hydrogel architecture and porosity. Hydrogel structure, mechanical properties, degradation, and molecular transport were characterized by SEM, swelling and degradation assays, rheology, and diffusion studies. Human brain organoids were embedded during the neural progenitor stage and subsequently differentiated within the hydrogels to evaluate their integration, viability, and maturation during long-term culture, using HA-methacrylate hydrogels and Matrigel as controls. FTIR and NMR confirmed successful HA functionalization, and the resulting hydrogels exhibited storage moduli ranging from 0.1 to 2.4 kPa, consistent with the reported mechanical range of CNS tissue. Modulation of PEG crosslinker molecular weight generated tunable network microarchitectures and markedly enhanced molecular transport, with diffusion coefficients for 70 kDa dextran up to eightfold higher in HA-norbornene hydrogels than in HA-methacrylate controls. Importantly, HA-norbornene matrices supported sustained brain organoid culture, neural cell integration, viability, and maturation while maintaining structural integrity over time. Together, these results demonstrate that PEG-tuned HA-norbornene hydrogels provide a defined and tunable extracellular environment that combines CNS-relevant mechanics with enhanced molecular transport, overcoming key limitations of conventional HA-based hydrogels while providing a more controlled and reproducible alternative to Matrigel. This platform offers a versatile matrix for long-term brain organoid culture with potential applications in neural disease modeling and drug testing.

Acknowledgments: We acknowledge the financial support from the European Union's Horizon Europe research & innovation program (EIC-2021-PATHFINDER-OPEN-01-01-101047099 4DBR) and Grants, PID2021-124839OA-I00,

PID2020-114407RA-100 and PID2024-159777OB-I00 funded by the Ministry of Science and Innovation of Spain (MCINAEI/10.13039/501100011033). Grant R01AG086270, funded by the National Institute on Aging of the National Institutes of Health (NIH); Grant P199, supported by the IRP Research Foundation. Funded by the European Union (ERC, 101230979 - SpineCraft) under the European Union's Horizon Europe research and innovation program. We acknowledge support from the Ramón y Cajal Program RYC2020-028732-I. Institutional support was provided by IBEC, which acknowledge the Centro de Excelencia Severo Ochoa (Grant CEX2023-001282-S, funded by MICIU/AEI/10.13039/501100011033).

References



[1] Kim, D. et al, 2026, 10.1038/s44385-025-00054-6.
[2] Axpe, E. et al, 2020, 10.1038/s41467-020-17245-x.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 56 presented by:

NAME: Carla Arroyo

Optimization of the Blocking Step for Label-Free prism SPR Detection of C5b-9 in Human Serum as a Biomarker of Neuromuscular Junction Damage in Myasthenia Gravis

Carla Arroyo-Rivera[1], Mehdi Torabi-Goodarzi[1], Javier Ramón[1]

Surface plasmon resonance (SPR) biosensors allow label-free, real-time detection of disease biomarkers, but their performance in complex biological matrices such as human serum is often compromised by nonspecific protein adsorption, which increases background signal and reduces both sensitivity and specificity. The terminal complement complex C5b-9 (membrane attack complex, MAC) is a promising biomarker of neuromuscular junction damage in myasthenia gravis (MG), where complement-mediated destruction of the postsynaptic membrane is a central driver of disease pathology. Reliable detection of C5b-9 directly in human serum therefore requires a sensor surface that minimizes nonspecific binding.

This work uses a home-built, prism-coupled, wavelength-interrogation SPR biosensor (Kretschmann configuration) developed within our group, based on a plasmonic gold-coated chip functionalized via amine coupling chemistry. Chips consist of glass coverslips of 10x20 mm, coated with a 1 nm chromium adhesion layer followed by 50 nm of gold. To optimize the blocking step prior to C5b-9 detection in real samples, four blocking agents are being evaluated — bovine serum albumin (BSA), SuperBlock, poly-L-lysine-graft-polyethylene glycol (PLL-PEG), and chicken serum. Blocking efficiency is assessed by monitoring the resonance wavelength shift ($\Delta\lambda$) associated with blocking agent deposition, and the residual $\Delta\lambda$ upon subsequent exposure to real undiluted sample, as a measure of nonspecific adsorption.

Based on the mechanisms reported in the literature — electrostatic repulsion between BSA and human serum albumin, and steric passivation by PEG-based polymers such as PLL-PEG — BSA and PLL-PEG are expected to outperform SuperBlock and chicken serum in reducing nonspecific adsorption from human serum on this gold-based SPR platform. Preliminary experiments comparing BSA and SuperBlock support this trend, with BSA showing better blocking performance. Focusing on BSA, a flow-rate optimization (5, 10, and 20 µL/min) identified a lower flow rate as more favorable for reducing nonspecific adsorption. The aim of this work is to identify the optimal combination of blocking agent and flow rate to enable reliable C5b-9 detection in real samples.

POSTER 57 presented by:
NAME: Carolina Tarantino

Modeling Ataxia-Telangiectasia Neurodevelopment Using an Optimized Isogenic Human Cerebral Organoid Platform

Carolina Tarantino[1], Marta Graells[1], Daniel Moya-Rull[1], Elena Garreta[1], Nuria Montserrat[1]

[1] Pluripotency for organ regeneration (PR Lab), Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.

Ataxia-Telangiectasia (A-T) is a severe autosomal recessive multisystem disorder caused by mutations in the ATM gene, characterized by progressive neurodegeneration, cerebellar ataxia, genomic instability, and cancer predisposition. Investigating the molecular neurodevelopmental etiology of A-T has been hampered by the limitations of currently available models, as animal models fail to fully reproduce the human neurodevelopmental phenotype and patient-derived induced pluripotent stem cell (iPSC) models are confounded by genetic background heterogeneity and variable differentiation capacity. Here, we report the establishment of a robust, optimized isogenic human embryonic stem cell (hESC)-derived cerebral organoid platform to model A-T neurodevelopment in a defined genetic background.

Using an inducible Cas9 hESC line (ES4-F51 iC2), we targeted clinically relevant mutation hotspots to generate complementary knock-out (KO) models: exon 6 frameshift mutations yielded an ATM-null model via complete protein loss, whereas exon 63 frameshift mutations generated a kinase-dead model expressing normal ATM protein levels lacking Ser1981 autophosphorylation upon radiation exposure. Both KO models preserved pluripotency while exhibiting hallmark cellular radiosensitivity and elevated micronucleus formation post-irradiation.

When subjected to standard unguided organoid differentiation, ES4-F51 WT and ATM KO lines displayed line-specific kinetics with delayed pluripotency exit compared to reference H9 hESCs, leading to disorganized apicobasal polarity, impaired tight-junction (ZO-1) alignment, and failure of neural rosette assembly. To overcome this differentiation bottleneck, we optimized the protocol by reducing initial cell seeding density (6,000 cells/organoid) and introducing transient dual-SMAD inhibition during days 2–5 of neural induction. This modification accelerated OCT4/NANOG downregulation, promoted uniform neuroectoderm specification (SOX1+, OTX2+), and restored polarized PAX6+ neural rosette architecture, enabling reproducible Matrigel embedding by day 7.

Extended maturation confirmed faithful sequential cortical lineage progression across all lines, marked by forebrain regionalization (FOXG1+), apical radial glia progenitors (PAX6+, SOX2+), intermediate progenitors (EOMES/TBR2+), and post-mitotic cortical neurons (DCX+, TUBB3+, TBR1+). This optimized platform minimizes line-dependent variability across defined developmental time-points up to day 100, establishing a highly reproducible isogenic framework for multi-stage RNA-sequencing transcriptomics, disease mechanism elucidation, and evaluation of targeted gene-reconstitution therapies in A-T.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 58 presented by:

NAME: Davide Arena

A Modular "Click" Hydrogel Platform for 3D Cell Culture and High-Throughput Screening

Davide Arena[1]; Aleixandre Rodrigo-Navarro[1]; Manuel Salmeron-Sánchez[1,2]

[1] Institute for Bioengineering of Catalonia (IBEC) The Barcelona Institute for Science and Technology (BIST) Barcelona 08028, Spain
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA) Barcelona, Spain

The extracellular matrix (ECM) presents cells with a dynamic mechanical landscape where viscoelasticity and stress relaxation dictate fundamental cellular processes. Replicating these mechanical cues in synthetic matrices remains a major bottleneck in 3D cell culture and mechanobiology due to the coupled properties of benchmarks like Matrigel and the rigidity of conventional synthetic hydrogels.[1]

To overcome these constraints, we present a modular platform engineered to navigate the mechanical property space -tailored for cell encapsulation- through a data-informed, optimization-driven design workflow. Our strategy leverages poly(pentafluorophenyl acrylate)s (PPFPAs) backbones of well-defined chain lengths that undergo post-polymerization modification with tailored primary amines.[2] Specifically, one precursor subset was functionalized with azide-bearing moieties, hydroxy-containing primary amines for hydrophilic balance and systematically changed loading percentages of aromatic units to foster hydrophobic associations. In addition, a complementary subset was decorated with dibenzocyclooctyne (DBCO) functional groups alongside with the hydrophilizing agents. With the reactive precursors in hand, we optimized the hydrogelation process, ensuring, on one hand, the maximum cell viability during *in situ* encapsulation, as well as a facile way to combinatorially generate a library of diverse materials.

The platform demonstrated excellent cytocompatibility. Exploiting SPAAC reactivity allowed precise, stoichiometric introduction of cell-adhesive motifs (e.g., RGD peptides). The resulting hydrogels successfully supported 2D and 3D culture of human mesenchymal stem cells, as well as 3D cellular spheroids.

Ultimately, we present a synthetic platform aimed at exploring and estimating viscoelastic moduli based on key molecular determinants—including degree of polymerization, hydrophobic content, and functional group density—which can be systematically tuned during the precursors' synthesis. By mapping these foundational constituent–property relationships, this workflow could potentially serve as a basis for integration with machine learning frameworks, offering a predictive guide for precursor design and the rational development of hydrogel libraries with targeted mechanical profiles.

References

1. a) Chaudhuri, O. *et al. Nature* **2020**, 584, 535 – 546. b) Chaudhuri, O. *et al. Nature Materials* **2016**, 15, 326 – 334. c) Aisenbrey, E. A.; Murphy, W. L. *Nature Reviews Materials* **2020**, 5, 539 –551. d) Gharios, R. *et al. Matter* **2023**, 6, 4195-4244.

2. a) Deng, L. *et al. Biomacromolecules* **2022**, 23 (1), 326–338. b) Liu, Y. *et al. J. Am. Chem. Soc.* **2015**, 137, 13096–13105. c) Grimm, A. *et al. Macromol. Rapid Commun.* **2025**, 2500264.

POSTER 59 presented by:
NAME: Ece Kutukcu

Influence of Mechanical Stimulation and Matrix Stiffness on Breast Cancer Cells

Ece Kutukcu[1], Francesca Mauro[1], Manuel Salmeron-Sanchez[1,2,3]

[1] Institute for Bioengineering Catalonia (IBEC), Barcelona Institute of Technology (BIST), Spain
[2] University of Glasgow, United Kingdom
[3] Institució Catalana de Recerca i Estudis Avançats (ICREA), Spain

Cells are capable of sensing and responding to changes in the mechanical properties of their extracellular matrix (ECM) through mechanosensing and mechanotransduction. Mechanical cues detected by cells through receptors like integrin, can activate certain pathways such as PI3K/AKT and thus regulate cellular processes including proliferation, survival, and migration. During breast cancer tumorigenesis, ECM components such as fibronectin and collagen deposit, resulting in the progressive stiffening of the tumor microenvironment. Changes in the mechanical properties of the environment have potential effects on the metastatic properties of cancer and its pathophysiological changes[1]. Although the effects of ECM stiffness on breast cancer cell behavior have been extensively investigated, the effects of external mechanical stimulation across different physiologically relevant ECM stiffnesses that mimic the mechanical changes occurring during tumor progression remain poorly understood.In this project we aim to understand how ECM stiffness and nanovibration collectively regulate breast cancer cell behavior and metastatic-associated properties. The study investigates how metastatic properties of the breast cancer cell line MCF7 change in regards of the 3D microenvironment stiffness that the cells are and how external nanovibration stimulation influences cell behavior. GelMA-based hydrogels with tunable stiffness were functionalized with polyethylene glycol-conjugated fibronectin (PEG-FN) to enhance cell and ECM interactions. MCF7 breast cancer cell spheroids were cultured within these 3D hydrogels of different stiffness. Three-dimensional tumor spheroids provide a more physiologically relevant model than commonly used 2D cultures by demonstrating accurate cell–cell interactions and cellular organization. Cancer spheroids were cultured under static and mechanically stimulated conditions to investigate how both hydrogel stiffness and mechanical stimulation affect cellular organization and behavior collectively. Preliminary results demonstrated that with the incorporation of PEG-FN increased cell–cell interactions and promoted the formation of a more interconnected cellular network.

[1] Gil-Redondo et al., “Substrate stiffness modulates the viscoelastic properties of MCF-7 cells”

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 60 presented by:

NAME: Eduard Torrents

Polymicrobial Interactions Involving *Burkholderia cenocepacia* Enhance Virulence, Alter Host Responses, and Modulate Antibiotic Tolerance in Cystic Fibrosis Infection Models

Júlia Alcàcer-Almansa[1,2], Joana Admella[1,2], Núria Blanco-Cabra[1,2,], Eduard Torrents[1,2,*]*

[1] Bacterial infections and antimicrobial therapies group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST). Baldiri Reixac 15-21. 08028 Barcelona, Spain.

[2] Microbiology Section, Department of Genetics, Microbiology and Statistics, Faculty of Biology, University of Barcelona, 643 Diagonal Ave., 08028, Barcelona, Spain.

Polymicrobial infections in the cystic fibrosis (CF) lung create complex microbial communities in which interspecies interactions profoundly influence pathogen behavior, disease progression, and therapeutic outcomes. Here, we investigated the interactions of *Burkholderia cenocepacia* with two clinically relevant CF pathogens, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, using a combination of planktonic cultures, biofilm models, and *in vivo* and cell-based infection systems. Across both microbial partnerships, coinfection resulted in enhanced pathogenicity compared with single-species infections, leading to increased host mortality in *Galleria mellonella* larvae and greater cellular damage in A549 epithelial cells. Distinct interaction dynamics were observed depending on the microbial community composition. In coinfections with *P. aeruginosa*, *B. cenocepacia* suppressed host immune responses and melanization, while both species exhibited increased expression of virulence-associated genes, contributing to accelerated disease progression and bacterial dissemination. In contrast, coculture with *S. aureus* triggered defensive adaptations in *B. cenocepacia*, including cellular aggregation and upregulation of adhesion- and iron acquisition-related genes, whereas *S. aureus* virulence gene expression remained largely unchanged. Biofilm analyses revealed that dual-species communities developed structured and spatially segregated architectures, with species-specific niche occupation under dynamic growth conditions. Furthermore, polymicrobial growth altered antimicrobial susceptibility profiles relative to single-species cultures, highlighting the limitations of conventional susceptibility testing in predicting treatment outcomes. Together, these findings demonstrate that the community context strongly shapes pathogen physiology, virulence, host-pathogen interactions, and antibiotic tolerance. Our work underscores the importance of incorporating polymicrobial interactions into experimental and clinical frameworks to better understand and manage chronic CF respiratory infections.

This study was supported by grants PID2024-158933OB-I00 funded by MCIN/AEI/10.13039/501100011033 and “ERDF A way of making Europe”; the CERCA programme and AGAUR-Generalitat de Catalunya (grant number 2021SGR01545), by the European Regional Development Fund (FEDER) and the Catalan Cystic Fibrosis association. E.T. is a researcher of the ICREA Academia 2025 program. J.A.A is thankful to MCIN for its financial support through a PRE2021–098703 grant funded by MCIN/AEI/10.13039/501100011033 and by the ESF “investing in your future”.

POSTER 61 presented by:

NAME: Emma Oriol

Two-photon polymerized anisotropic microarchitectures for cardiomyocyte guidance

E. Oriol-Ferrero[1,2], E. Yanac-Huertas[3,1], P. Ferrando[1], B. Borges-Fernandes[1], B. Suárez- Villacres[1], E. Engel[5,3,4], R. Rodríguez-Trujillo[1,2,4], O. Castaño[1,2,3,4]

[1] *Electronics and Biomedical Engineering, UB, 08028, Barcelona, Spain*
[2] *Institute of Nanoscience and Nanotechnology, UB, 08028, Barcelona, Spain*
[3] *Biomaterials for Regenerative Therapies, IBEC, BIST, 08028, Barcelona, Spain*
[4] *CIBER-BBN, 28029, Madrid, Spain*
[5] *Materials Sciences and Engineering, UPC, 08930 Barcelona, Spain*

Cardiac tissue engineering requires platforms reproducing the alignment of native myocardium, attainable in 2D but challenging in 3D. Here, two-photon polymerization (2PP) fabricates anisotropic substrates and scaffolds for cardiomyocyte guidance.

Three architectures were fabricated by 2PP and characterized by scanning electron microscopy (Fig. 1). These were designed to progressively increase topographical complexity from planar to fully three-dimensional geometries. Finite element analysis was used to validate the scaffold mechanical design prior to fabrication.

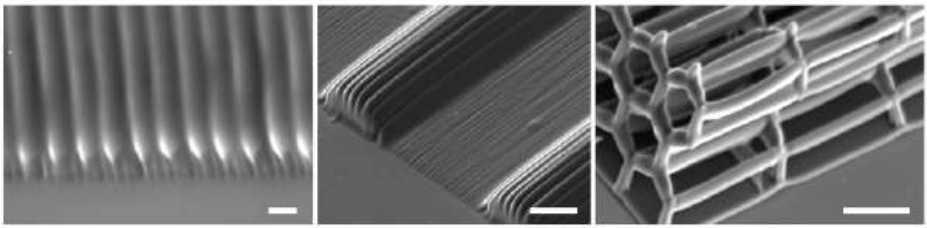


Figure 1. Scanning electron microscopy images of 2PP microfabricated structures. (A) Grating pattern. (B) Semi-cylindrical pattern with secondary grating pattern. (C) 3D honeycomb scaffold. Scale bars: 1µm (A), 5µm (B), 50µm (C).

HL-1 cardiomyocytes were cultured on linear and semi-cylindrical gratings, stained for α-actinin, and imaged by confocal microscopy. Tensor-based image analysis preliminary results showed that circular variance index increased from 0.884±0.05 in controls to 0.478±0.2 on linear gratings and 0.69 ± 0.03 semi-cylindrical gratings.

Overall, these findings demonstrate that 2PP-fabricated anisotropic microarchitectures can reproduce key structural cues of the native myocardium and direct cardiomyocyte alignment, providing a basis for future 3D cardiac tissue models.

Acknowledgements We acknowledge financial support from grants PID2021-124575OB-I00 and PID2024-159777OB-I00, funded by MICIU/AEI/10.13039/501100011033, and from grant PREP2024-003092, funded by MICIU/AEI/10.13039/501100011033 and by FSE+. We also acknowledge funding from the European Union's Horizon Europe programme under grant agreement No. 101047099, and from Torró Solidari (Torrons Vicens-RAC1).

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 62 presented by:

NAME: Eulàlia Dou

From Prototypes to Production: A Scalable Blood–Brain Barrier-on-a-Chip for Pharmaceutical Screening

Eulàlia Negre[1], Anna Lagunas[1,2], Mònica Mir[1,2,3]

[1] Nanobioengineering group, Institute for Bioengineering of Catalonia (IBEC) Barcelona Institute of Science and Technology (BIST), 12 Baldiri Reixac 15-21, Barcelona 08028, Spain,

[2] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina, Instituto de Salud Carlos III, Barcelona, Spain

[3] Department of Electronics and Biomedical engineering, University of Barcelona, Martí i Franquès 1, 08028 Barcelona, Spain.

The development of robust, scalable blood–brain barrier-on-a-chip (BBB-oC) models is essential for bridging the gap between preclinical drug screening and clinical outcomes. Current limitations, primarily rooted in the reliance on polydimethylsiloxane (PDMS) for prototyping, hinder large-scale industrial adoption and reproducibility. This study aims to validate a high-fidelity BBB-oC platform for pharmaceutical applications by correlating real-time optical permeability measurements with gold-standard liquid chromatography-mass spectrometry (HPLC-MS) and transitioning device fabrication to scalable thermoplastic polymers.

The performance of the BBB-oC model was assessed using two reference compounds, quinacrine and doxorubicin. Barrier permeability was evaluated concurrently via real-time fluorescence imaging and quantitative HPLC-MS analysis of samples collected from the luminal and abluminal chambers. To enhance industrial manufacturability, we compared hot embossing replication fidelity in Poly-(methyl methacrylate) (PMMA), and Flexdym against traditional PDMS casting. Finally, we expanded the therapeutic screening panel to include clinical drugs: fluoxetine, donepezil, L-Dopa, and levetiracetam.

Comparative analysis demonstrated high agreement between real-time imaging and HPLC-MS permeability coefficients, validating the optical quantification method. HPLC-MS profiling yielded distinct permeability values for the test panel: Donepezil ($7.47 \cdot 10^{-6}$ cm/s), Fluoxetine ($8.57 \cdot 10^{-6}$ cm/s), L-Dopa ($4.73 \cdot 10^{-6}$ cm/s), Doxorubicin ($4.33 \cdot 10^{-6}$ cm/s), Levetiracetam ($3.06 \cdot 10^{-6}$ cm/s), and Quinacrine ($2.89 \cdot 10^{-6}$ cm/s). Good concordance was observed between the *in vitro* permeability profiles and *in vivo* assay results regarding the barrier penetration of the evaluated compounds. Manufacturing studies revealed variability in post-length replication across PMMA and Flexdym substrates, providing critical parameters for process optimization.

This work validates the BBB-oC as a precise tool for pharmacokinetic screening and demonstrates that thermoplastic hot embossing is a viable path toward scalable, industrial-grade production. These advancements facilitate the transition from laboratory prototypes to high-throughput, reproducible platforms capable of supporting pharmaceutical drug development pipelines.

Keywords: Blood-brain barrier, Organ-on-a-chip, Pharmacokinetics, HPLC-MS, Hot embossing, Scalable manufacturing, Drug screening.

POSTER 63 presented by:

NAME: Eva Garrido

Engineered Human Spinal Cord Constructs using 3D-bioprinting Technologies and iPSC-Derived Cells

Garrido E[1], Louail A[1], Barceló X[1], Chandravanshi P[1], Saez F[1], Ena GF[1], Ortega JA[4,5], Álvarez Z[1,2,3]

[1] Biomaterials for Neural Regeneration Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain

[2] CIBER en Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Madrid, Spain

[3] Simpson Querrey Institute for BioNanotechnology, Northwestern University, Chicago, Illinois, USA

[4] Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), L'Hospitalet del Llobregat, Spain

[5] Department of Pathology and Experimental Therapeutics, Institute of Neurosciences, University of Barcelona, L'Hospitalet de Llobregat, Spain

Understanding the pathophysiology of spinal cord (SC) injury and related neurological disorders, and enabling the development of restorative therapies, requires advanced human-relevant in vitro models that faithfully recapitulate the structural and cellular complexity of the human SC. Here, we address this unmet need by engineering biofidelic human SC constructs that integrate state-of-the-art bioprinting technologies with biologically instructive biomaterials to recapitulate tissue architecture and function at a clinically relevant scale. Our strategy is based on two complementary and tightly integrated approaches: (i) engineering an anatomically accurate SC exoskeleton, and (ii) generating and spatially organizing the key cellular populations of the human SC.

Using MRI-derived anatomical reconstructions and volumetric printing, we fabricated biomimetic exoskeletons that faithfully replicate the dimensions and compartmentalization of human SC, including the white and grey matter regions. The constructs, that can be printed within seconds, are customizable to represent cervical, thoracic and lumbar spinal segments, feature tunable porosity, and provide a structural framework that guides cell positioning and tissue organization. Within this engineered scaffold, we precisely integrate the human induced pluripotent stem cell (iPSC)-derived neural, glial and vascular populations through spatially controlled inkjet bioprinting, recreating their native anatomical distribution.

This work lays the foundation for the next generation of human spinal cord models, opening new opportunities to study tissue development, model neurological disorders, and accelerate the translation of regenerative therapies.

Acknowledgements: Supported by grants EU funding (ERC, 101230979 – SpineCraft, Horizon Europe), PID2024-162574OB-I000 (10.13039/501100011033, ERDF/EU), R01AG086270 (NIA, NIH), and P199 (IRP Research Foundation); fellowships/programs JDC2023-051798-I (Juan de la Cierva, MICIU/AEI/10.13039/501100011033, ESF+), RYC2020-028732-I (Ramón y Cajal).

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 64 presented by:

NAME: Gal·la Vinyes i Bassols

Glycocalyx remodeling at the blood-brain barrier: a microfluidic murine model to study cell-membrane protein endocytic dynamics

Gal·la Vinyes-Bassols[1,2], Álvaro Morellá-Campos[1,2], Josep Samitier[1,2], Giuseppe Battaglia[1,3], Daniel González-Carter[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.
[2] University of Barcelona (UB), Barcelona, Spain.
[3] Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain.

The blood–brain barrier (BBB) is a highly selective vascular interface that restricts molecular and cellular exchange between the bloodstream and the brain. This selectivity arises from the specialized properties of brain microvascular endothelial cells (BMECs), particularly their cell-membrane proteins, whose function depends on both abundance and residency time on the cell membrane[1]. Although the identity and abundance of BBB cell-membrane proteins have extensively been characterized, their endocytic turnover rates (ETOR, the dynamics contemplating internalization, recycling and degradation) governing the BBB physiology remains poorly understood. Our previous work revealed tissue-specific differences in endothelial membrane-protein endocytic rates, prompting us to ask which features of the brain endothelial microenvironment regulate cell-membrane protein endocytosis[2].

The endothelial glycocalyx, a dense coat of glycans and glycoconjugates lining the luminal surface of blood vessels, is emerging as a key regulator of membrane-protein dynamics. The glycocalyx can both inhibit endocytosis via steric hinderance and promote it through protein clustering[3,4]. Specifically, BMECs possess a uniquely thick, negatively charged glycocalyx enriched in sialic and hyaluronic acids, yet its role in controlling BBB function remains largely unexplored[5,6]. We therefore hypothesize that glycocalyx composition modulates cell-surface protein endocytosis and sought to test this under physiologically relevant flow conditions, given that hemodynamic forces strongly regulate glycocalyx structure and organization.

To this end, we developed a two-compartment microfluidic platform that supports the formation of a confluent BMECs monolayer and enables quantitative assessment of cell-surface protein internalization. Preliminary results confirm successful BMEC seeding and the establishment of a functional barrier that restricts the passage of 4 kDa dextran. We further demonstrate controlled enzymatic removal of glycocalyx sialic acids. Ongoing work will extend these experiments to additional glycocalyx-targeting enzymes and systematically characterize their effects on membrane-protein endocytic turnover. Collectively, this study provides a dynamic, flow-based platform to dissect how glycocalyx remodeling regulates membraneprotein trafficking at the BBB.

Main references:

1. Porro, G. M. *et al.* Identifying molecular tags selectively retained on the surface of brain endothelial cells to generate artificial targets for therapy delivery. *Fluids Barriers CNS* **20**, (2023).

2. Tomás-Sitjes, A. *et al.* Endocytic turnover of endothelial cell-membrane proteins as a driver of rat blood-brain barrier specialization and dysfunction. *iScience* **29**, (2026).

3. Gollapudi, S. *et al.* Steric pressure between glycosylated transmembrane proteins inhibits internalization by endocytosis. *Proc. Natl. Acad. Sci. U. S. A.* **120**, e2215815120 (2023).

4. MacDonald, E. *et al.* Growth factor-triggered de-sialylation controls glycolipid-lectin-driven endocytosis. *Nat. Cell Biol.* **27**, 449–463 (2025).

5. Larsen, R. *et al.* Multi-omic analysis reveals the unique glycan landscape of the blood-brain barrier glycocalyx. *bioRxiv* https://doi.org/10.1101/2025.04.07.645297 (2025) doi:10.1101/2025.04.07.645297.

6. Shi, S. M. *et al.* Glycocalyx dysregulation impairs blood-brain barrier in ageing and disease. *Nature* **639**, 985–994 (2025).

POSTER 65 presented by:
NAME: Inass Himmiche

Ocular mechanism with embedded visual sensing for biohybrid robotics

Inass Himmiche[1], Florencia Lezcano[1], Marina Rovira[1], Samuel Sánchez[1,2]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.

Biohybrid robotics combines biological components, such as muscle-based bioactuators (MBs), with artificial engineered systems. While MBs have been widely applied to locomotion, manipulation and grasping platforms, their integration into anatomically bioinspired, sensory-organ architectures, such as an eye capable of directional motion and visual perception, remains largely unexplored. Addressing this gap, we present a biohybrid robotic eye mechanism that couples musculoskeletal actuation with embedded visual sensing. The system was designed in three modules: a mechanical skeleton with MBs, an embedded sensing unit connected to a computer vision algorithm, and a stimulation platform. A CAD-designed skeleton mechanically coupling the ocular component to the bioactuators was 3D-printed using biocompatible materials and assembled into a functional prototype (Fig. 1). A microcamera was installed inside the eyeball to capture live video processed in real time using computer vision for movingobject identification and tracking. In parallel, C2C12-based 3D-printed MBs were fabricated and successfully integrated onto the prototype. To validate the structural module, a kinematic characterization assessed muscle contraction and ocular rotation by recording and postprocessing the prototype's movement under electrical stimulation of one MB, showing preliminary rotations of approximately 32°, around 71% of the human oculomotor range. The sensing module was validated separately, successfully achieving object tracking; connecting it to the stimulation module for closed-loop control remains future work. Together, these results support the modular design of the skeleton, bioactuator and sensing units, laying the structural foundation for a fully bioprinted, multibioactuator biohybrid eye capable of autonomous, closed-loop object tracking.

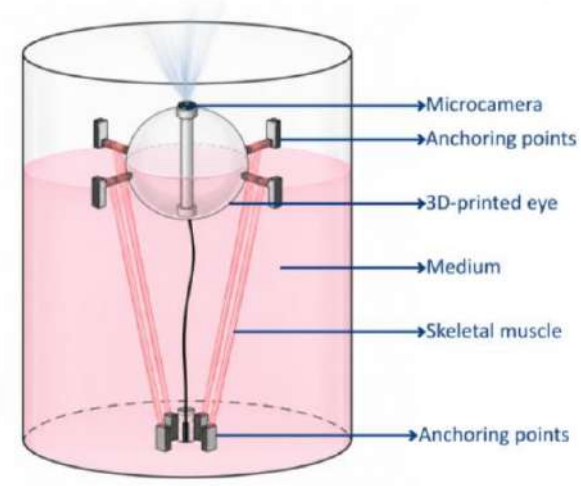


Fig.1 Schematics of the biohybrid robotic eye.

POSTER 66 presented by:

NAME: Inés Martínez Soria

Modulation of Hippocampal Vulnerability and Synaptic Plasticity by Adgrd1/GPR133 in Adult Mice

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

[1] *Molecular and Cellular Neurobiotechnology, Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Science Park of Barcelona, Barcelona, Spain.*
[2] *Department of Cell Biology, Physiology and Immunology, Faculty of Biology, University of Barcelona, Barcelona, Spain.*
[3] *Ciberned (Network Centre of Biomedical Research of Neurodegenerative Diseases), Institute of Health Carlos III, Barcelona, Spain.*
[4] *Institute of Neurosciences, University of Barcelona, Barcelona, Spain.*
[5] *August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain.*
[6] *Neurophysiology Laboratory, Department of Biomedicine, Faculty of Medicine, University of Barcelona, Barcelona, Spain.*
[7] *Institut Químic de Sarrià (IQS), Universitat Ramon Llull (URL), Barcelona, Spain.*
[8] *Institute for the Science of the Aging Brain (ISAB), St. Gallen, Switzerland.*

The adhesion G protein-coupled receptor GPR133 (Adgrd1) has been implicated as a potential regulator of neuronal stability and synaptic function. This study investigated its role in neuronal development, synaptic plasticity, and vulnerability to neurodegeneration. Using Adgrd1-deficient mice (*Adgrd1*$^{0/0}$) and a combination of histological, molecular, electrophysiological, and behavioral approaches, we examined how loss of GPR133 impacts neuronal homeostasis. Behaviorally, *Adgrd1*$^{0/0}$ mice exhibited impaired nest building, reduced object exploration, and increased immobility. Electrophysiological recordings revealed a trend toward reduced long-term potentiation (LTP), indicating early functional synaptic impairments in the absence of detectable structural alterations. *Adgrd1*$^{0/0}$ mice also displayed increased susceptibility to kainate (KA)-induced excitotoxicity, accompanied by early hippocampal neurodegeneration, pronounced glial reactivity, and inflammatory responses. Molecular analyses provided further insight into the mechanisms underlying this heightened vulnerability. RNA-seq analysis identified elevated expression of *Snca* (α-synuclein), a gene associated with synaptic dysfunction and neurodegenerative processes, alongside reduced expression of *Gabra2* and *Wdfy1*. Together, these transcriptional changes point to impaired GABAergic signaling, altered autophagy-related pathways, and dysregulated inflammatory responses. In summary, these findings suggests that GPR133 deficiency is associated with increased vulnerability to excitotoxic injury and with molecular changes affecting synaptic and stress-related pathways. While the precise mechanisms remain to be fully elucidated, the combined behavioral, electrophysiological, and transcriptomic alterations indicate that GPR133 may contribute to maintaining neuronal resilience. Taken together, the data point toward a multifactorial phenotype in which altered signaling networks may interact to shape neuronal vulnerability.

POSTER 67 presented by:
NAME: Jakub Podraza

Integrating Microphysiological Systems and Longitudinal HP-MRI in Ovarian Cancer Modeling

Jakub Podraza, Vicent Ribas Serra, Irene Marco Rius
Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

High-Grade Serous Ovarian Carcinoma (HGSOC) is a highly lethal malignancy characterized by late-stage diagnosis, transcoelomic metastasis, and unique metabolic shifts [1]. Driven by the Warburg effect, HGSOC cells prioritize aerobic glycolysis, rapidly elevating lactate production to survive and proliferate [5]. Current preclinical modeling struggles to capture this dynamic tumor microenvironment; traditional *in vitro* cultures lack complex tissue architecture, while animal models often fail to perfectly replicate human-specific responses [1]. This study outlines a dual-strategy methodology to bridge the translational gap between simple cell cultures and complex *in vivo* environments.

To replicate the complex HGSOC microenvironment, we aim to engineer an Organ-on-a-Chip (OoC) platform by seeding murine ID8 cells directly onto MRI-compatible carboxymethylcellulose (CMC) scaffolds. This non-destructive, radiation-free imaging modality amplifies the magnetic resonance signal of ^{13}C-labeled biomolecules by up to 10.000 times [3]. By introducing HP [1-^{13}C]pyruvate into both the perfusable OoC system and a murine model (C57BL/6J mice injected with ID8 cells), we will continuously track its intracellular conversion into [1-^{13}C] lactate in real time [3,5]. This longitudinal approach maps metabolic fluxes long before structural tumor changes occur [2,5].

While preliminary data acquisition is ongoing, expected outcomes include establishing highly accurate, translatable preclinical models that validate non-destructive HP-MRI readouts against traditional histopathological and enzymatic assays. Crucially, by cross-validating metabolic dynamics between microphysiological systems and *in vivo* subjects, this methodology actively promotes the 3Rs principle, driving Replacement through bioengineered tissue platforms and Reduction via longitudinal imaging that eliminates the need to sacrifice separate cohorts at intermediate timepoints [4].

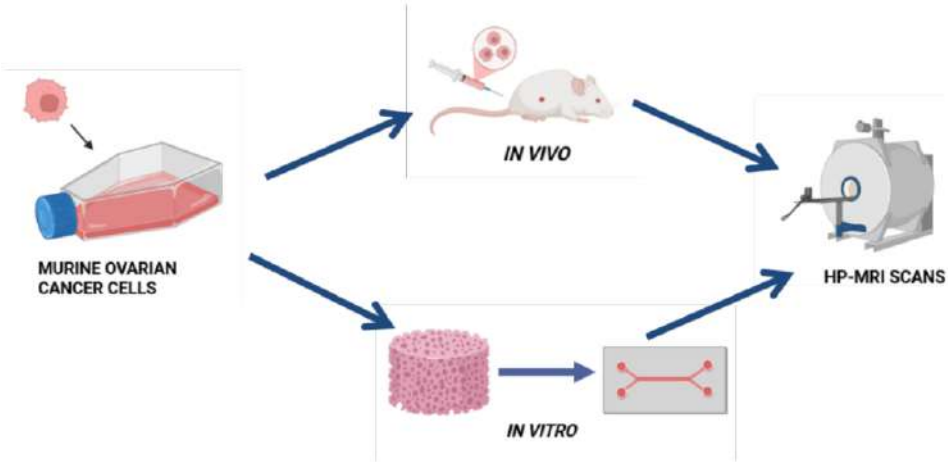


Figure 1: Dual in vivo and in vitro modeling strategy for non-invasive HP-MRI tracking of HGSOC metabolic dynamics.

Bibliography:

1. Flörkemeier, I., Antons, L.K., Weimer, J.P. et al. Multicellular ovarian cancer spheroids: novel 3D model to mimic tumour complexity. Sci Rep 14, 23526 (2024).

2. Kurhanewicz, John et al. Hyperpolarized ^{13}C MRI: Path to Clinical Translation in Oncology. *Neoplasia (New York, N.Y.)* vol. 21,1 (2019): 1-16.

3. Mangas-Florencio, Lluís et al. "A DIY Bioreactor for in Situ Metabolic Tracking in 3D Cell Models via Hyperpolarized ^{13}C NMR Spectroscopy." *Analytical chemistry* vol. 97,3 (2025): 1594-1602. 4. Marco-Rius I, Jensen PR, Bertelsen LB. Hyperpolarised magnetic resonance spectroscopy with lab-on-a-chip disease models. *Dis Model Mech*. 2026;19(6):dmm052817.

5. Woitek, R., & Gallagher, F. A. (2021). The use of hyperpolarised 13C-MRI in clinical body imaging to probe cancer metabolism. British Journal of Cancer, 124(7), 1187-1198.

POSTER 68 presented by:
NAME: Johannes Gschwind

Generation and characterization of SALL1 and GATA3 knock-out human pluripotent stem cell lines for studying kidney development and disease

Johannes Gschwind[1], Daniel Moya-Rull [1], Carolina Tarantino [1], Elena Garreta[1], Nuria Montserrat [1]

[1] Pluripotency for organ regeneration (PR Lab), Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.

Human pluripotent stem cells (hPSCs) can self-organize and differentiate into threedimensional organoids, providing a powerful platform to study human development and disease. Combined with precise genome-editing approaches, hPSC-based models enable the investigation of gene function and disease mechanisms. In our laboratory, we developed hPSC lines that express Cas9 upon doxycycline treatment, named iC2 platform. In the present work, we exploited this system to generate knock-out (KO) hPSC lines to investigate the roles of SALL1 and GATA3 during kidney differentiation. Both genes are involved in early kidney development, and their mutations are associated with congenital anomalies of the kidney and urinary tract (CAKUT). The parental ES[4] iC2/+ 51 hPSC line was used to generate SALL1 and GATA3 KO clones, together with their corresponding wild-type (WT) control clones. The generated KO and WT clones were characterized to confirm the maintenance of pluripotency by qPCR and immunofluorescence analysis of pluripotency-associated markers. Subsequently, SALL1 and GATA3 KO and WT clones were differentiated into kidney organoids using a stepwise differentiation protocol, previously published by our laboratory, under free-floating culture conditions. Loss of SALL1 and GATA3 expression in KO clones was assessed by immunofluorescence and western blot analysis at different time points throughout kidney organoid differentiation, using WT clones as controls. The resulting organoids were further characterized at different stages of differentiation using histological, molecular, and protein-based approaches. Hematoxylin and eosin staining was performed to assess the development of renal vesicles at day 11 and nephron-like structures at day 20 of differentiation. The expression of SALL1, GATA3, and relevant renal cell markers was assessed by immunofluorescence and confocal imaging, with quantitative image analysis to determine the proportions of different renal cell populations. In addition, qPCR analysis was performed to assess the expression of renal developmental markers, key target genes for SALL1 and GATA3, and late-stage nephron markers in WT and KO organoids. Altogether, these approaches enabled the characterization of SALL1- and GATA3-deficient kidney organoids and established a platform to investigate the roles of these genes during kidney development and for in vitro modeling of CAKUT.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 69 presented by:

NAME: Jose Huguet

Development of Barrier-Free Cancer-on-Chip Microfluidic Platforms for Studying the Cancer-Immunity Cycle in Colorectal Cancer

Jose Huguet-Suarez[1], David Bartalomé-Català[1], María García-Diaz [2,3], Núria Torras [2,3], Jordi Comelles [2,3], Elena Martinez[1,2,3,4]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST)
[2] Fraunhofer Center of Applied Theragnostics (Fraunhofer-CAT), Barcelona, Spain
[3] Department of Electronics and Biomedical Engineering, University of Barcelona (UB)
[4] Centro de Investigación Biomédica en Red (CIBER)

Colorectal cancer (CRC) is one of the most common cancers worldwide and is a leading cause of cancer-related mortality. Despite therapeutic advances, the efficacy of treatments for solid tumors remains limited. Current *in vitro* CRC models have important limitations, as they do not adequately recapitulate the complexity of the tumor microenvironment or the physiological barriers that immune cells must cross. The development of a microfluidic chip capable of simultaneously reproducing the tumor microenvironment, vascular and lymphatic barriers, and chemotactic gradients will enable the physiologically relevant study of immune cell migration throughout the cancer-immunity cycle in CRC and enhance drug development.

This microfluidic chip includes a central chamber which recapitulates the tumor microenvironment (TME, including hydrogel, human intestinal fibroblasts and cancer spheroids, as well as 2 lateral chambers representing the endothelial and lymphatic vessels. Additionally, in contrast to most common *in vitro* gut models, the chips developed in this study are barrier-free, establishing a continuous, unobstructed gel–media interface that facilitates molecular exchange over a large interfacial area with minimal interference by using phase-guides.

Different chip geometries, with varying dimensions of phase guide width and height were microfabricated using 3D replica molding and photolithography techniques and refined to adequately confine the hydrogel (Matrigel-Collagen mixture) and ensure its full polymerization. Furthermore, diffusion trials, ICC and cytoxicity assays were carried out to characterize the functionality of the chip, demonstrating its ability to recapitulate the intestinal barrier *in vitro*.

This barrier-free CRC platform may provide further insight into the mechanisms underlying immune cell migration, tumor–immune interactions, and therapeutic response within the tumor microenvironment, supporting the development and evaluation of novel therapeutic strategies for colorectal cancer.

POSTER 70 presented by:

NAME: Júlia Fabà Costa

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

Julia Fabà-Costa[1], Amélie L. Godeau[1], Marc Casals[1], Ot Massafret[1], Anna Ferrer-Vaquer[1], Anna Seriola[1], Miquel Solé[2], Montse Boada[2], Samuel Ojosnegros[1].

[1] Bioengineering in Reproductive Health, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), 08028 Barcelona, Spain.

[2] Reproductive Medicine Unit, Department of Obstetrics, Gynaecology and Reproduction, Dexeus Mujer, Hospital Universitari Dexeus, 08028, Barcelona, Spain.

Infertility affects approximately 15% of reproductive-aged couples worldwide. Embryo implantation is a critical step in successful pregnancy, as most conceptions are lost at this stage and only one-third result in a live birth. This natural inefficiency has not been significantly improved by assisted reproductive technologies, highlighting the need to better understand the events controlling human conceptus formation and development during implantation.

Traditional static in vitro embryo culture systems poorly replicate the dynamic environment of the uterus, leading to reduced embryo viability and limited peri-implantation development. Dynamic culture systems, in contrast, mimic better in vivo conditions and may enhance embryo quality and implantation rates. However, existing dynamic systems primarily focus on pre-implantation embryo culture and are often limited to specific windows of embryonic development.

Here, we propose a microfluidic embryonic culture platform that enables the establishment of a dynamic culture system compatible with time-lapse imaging. This platform allows us to optimize conventional culture conditions and adapt gas and nutrient supply according to the developmental stage of the embryos, while also facilitating the removal of waste products. The device is fabricated using replica molding and consists of a culture platform with an integrated hydrogel layer on which embryos can implant.

Mouse embryos were cultured from the blastocyst to early gastrulation stages. They displayed implantation morphology consistent with the literature and expressed Oct4, a marker of the embryonic epiblast, precursor of the future fetus, and Cdx2, a marker of the trophectoderm, precursor of extraembryonic tissues contributing to the placenta.

The platform was also adapted for human embryo culture. Following blastocyst thawing, human embryos were cultured for 72 hours and developed and implanted similarly to controls, forming both epiblast and hypoblast layers, which give rise to the fetus and extraembryonic tissues, respectively.

Overall, we developed a versatile microfluidic platform enabling dynamic culture and live monitoring of mouse and human embryos through peri-implantation development. By providing controlled access to this otherwise experimentally inaccessible developmental window, this platform is a powerful approach to investigate the mechanisms governing human implantation and early embryogenesis.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 71 presented by:

NAME: Keerthy Reghunandanan

Dissecting chemokine driven cell migratory behaviour of breast cancer in a 3D Micro physiological system using a custom developed migration tracker

Keerthy Reghunandanan [1], Javier. G. Fernandez[2]*

[1] Engineering Product Development (EPD) Pillar, Singapore University of Technology and Design, 8 Somapah Road, Singapore
[2] Bio integrated Materials and Engineering, Institute for Bioengineering of Catalonia, Barcelona, Spain*

Cell migration guided by chemical gradients (chemotaxis) is a fundamental process from embryonic development immune responses, and cancer metastasis. In cancer, different tumor types exhibit organ-specific patterns of metastasis, suggesting that dissemination is not random but a pre-programmed event influenced by biochemical cues within the tumor microenvironment. The transition of tumor cells toward a metastatic phenotype is tightly regulated by chemokine gradients and their interactions with surrounding stromal and immune cells. Therefore, elucidating the chemotactic pathways that drive preferential cancer cell migration is essential for identifying therapeutic strategies that interrupt early metastatic events. By simulating this interaction in tumor-on-chip systems, medical professionals can learn about other approaches to treatment that can block the chemical sources that cause cancer invasion.

Here, we propose an integrated approach combining a flow-free, 3D micro-physiological chemotaxis platform with a custom developed cell migration tracker capturing migration behavior of breast cancer cells under different controlled chemokine stimuli. The microfabricated device generates stable, long-lived chemokine gradients within a 3D ECM-like matrix without inducing shear stress, enabling physiologically relevant, long-term, high-resolution imaging of cell dynamics. Studying cell migration in 3D microenvironments requires not only physiologically relevant models but also powerful analytical tools to handle the large volumes of time-resolved imaging data generated during migration assays. To address the challenges posed by large, time-resolved imaging datasets, we developed a computer vision–based analysis workflow incorporating deep-learning segmentation and robust tracking algorithms. This automated pipeline extracts quantitative migration metrics with reduced user bias and improved reproducibility compared to conventional manual or semi-manual methods. Overall, the study aims to improve our ability to predict metastatic potential and evaluate anti-metastatic treatments by observing not just where and how fast individual cells move, but *how* they move together.

POSTER 72 presented by:
NAME: Lluís Mangas Florencio

Hyperpolarised ^{13}C NMR enables functional drug response assessment in early-stage oncology drug development

Lluís Mangas-Florencio[1], Vicent Ribas[1], Teresa Royo Bargués[2], Maria A Ortega[1], Irene Marco-Rius[1]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Spain.
[2] School of Medicine UB-IDIBAPS and TEMA Therapeutics, S.L., Barcelona, Spain

The process of drug development is slow and costly, taking around 10 to 15 years for a drug to reach the market[1]. The high attrition rates of drug candidates during clinical trials highlights the limitations of current preclinical models. Both animal and conventional in vitro cell culture systems have a limited predictive capacity for human toxicity, metabolism and efficacy[2].

For this reason, drug development needs new approaches and tools to provide more predictive assays. Organs-on-a-Chip (OoC) mimic the physiology and functionality of human organs and have the potential for accurate analysis of functional disability, toxicity profiles or compound efficacy[3]. Magnetic Resonance (MR) enables the analysis of molecular composition and dynamics, yet is hampered by low sensitivity. ^{13}C nuclear spin hyperpolarisation (HP) techniques enhance signal intensity by 10,000-fold[4]. In this work, we combine OoC platforms with HP-MR spectroscopic imaging to study the drug response in early-stage drug development workflows in real-time and non-destructively in a parallel manner.

We evaluated the use of HP-NMR across multiple cellular models and early-stage drug candidates in collaboration with biotechnology partners seeking metabolic insight to guide compound prioritisation. We measured the conversion from HP [1-^{13}C]pyruvate to HP [1-^{13}C]lactate, as an indicator of the Warburg effect, a hallmark of cancer metabolism. In a 3T preclinical MRI scanner (Bruker) we used chemical shift images for static spatially resolved measurements or sequential selective single pulses for temporal data.

In the first case study, we aimed to confirm the mechanism of action of a candidate compound previously suggested to directly modulate the Warburg phenotype and cancer cell metabolic machinery. In the second case study, we assessed the impact of a distinct candidates on Warburg-associated pathways. The HP-NMR experiments revealed the importance of analysing the effect of drug treatment in live cells to characterise the behaviour under the real crowded microenvironment and cellular contextualisation.

[1] Hinkson, IV, et al. Front Pharmacol 11, 770 (2020); [2] Esch, EW, et al. Nat Rev Drug Discov 14, 248–260 (2015); [3] Jodat, YA, et al. Curr Pharm Des 24, 5471–5486 (2018); 4 Mangas-Florencio, L, Herrero-Gómez, A, *et al. Anal Chem* **97**, 1594–1602 (2025).

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 73 presented by:

NAME: Marc Riu-Villanueva

An assembloid model to interrogate the contribution of inhibitory cortical interneurons to familial Alzheimer's disease network alterations

Marc Riu-Villanueva [1,2,3,4], Karolina Zimkowska [1,2,3,4] and José Antonio del Río [1,2,3,4].

[1] Molecular and Cellular Neurobiotechnology, Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Science Park of Barcelona, 08028 Barcelona,

[2] Department of Cell Biology, Physiology and Immunology, Faculty of Biology, University of Barcelona, 08028 Barcelona, Spain

[3] Network Center for Biomedical Research of Neurodegenerative Diseases (CIBERNED), Institute Carlos III, Ministry of Health, 08028 Barcelona, Spain

[4] Institute of Neuroscience, University of Barcelona, 08035 Barcelona, Spain

Familial Alzheimer's disease (fAD) accounts for around 1-5% of AD cases. Compared to sporadic AD, It is characterized by an early onset, a quicker pathology progression and is directly linked to mutations affecting Amyloid processing. Pathophysiologically, it's characterized by the accumulation of amyloid-β (Aβ) aggregates, their evolution into senile plaques, and a progressive aggregation of pathological tau, irreversibly causing neuronal death and inflammation.

Before these neuropathological hallmarks appear, early neuronal network dysfunctions have been described in fAD patients, as well as in mouse and in vitro models. These include an imbalance between excitatory and inhibitory synaptic activity, which leads to a hyperexcitable system. Cortical inhibitory interneurons are deeply involved in the regulation of neuronal activity, and its dysfunction has been linked to AD functional alterations. However, the origin, nature, and cellular dysfunction responsible for these alterations remain largely unclear. Here, we want to address this scenario with novel 3D stem-cell models, trying to mimic the fAD brain. Would carrying fAD-related mutations in inhibitory interneuron lineages alone affect the network's activity? Would it have an additive effect on excitatory lineages?

With the development of human induced pluripotent stem cell-derived (hiPSC) organoid technologies, it is possible to generate human in vitro 3D tissue with diverse cellular identities and complex neuronal activity. Taking advantage of the distinct developmental origin and trajectory of cortical interneurons, which are generated in the Subpallium (SP) and migrate to the cortex (CO), assembloids of SP and CO models can be generated that contain an enhanced inhibitory neuron population. Mixed assembloids can then be generated by fusing SP organoids from fAD hiPSCs with cortical organoids from wild-type (WT) hiPSCs or vice versa, alongside WT:WT and fAD:fAD assembloids. These mixed assembloids will allow the dissection of how pro-amyloidogenic mutations in cells from either origin affect the overall cortical network activity and fAD pathophysiology.

We generated hiPSC-derived CO and SP organoids from hiPSCs with a fAD mutation in the PSEN1 gene (A246E). CO organoids express forebrain and cortical neuronal markers, while SP organoids express transcription factors typical of SP-born neuronal progenitors. After immunostaining, fAD cortical organoids show increased Aβ aggregation compared to WT. The baseline global and individual neuronal activities are being evaluated in organoids and assembloids using genetically encoded calcium indicators (GECI) and 3D micro-electrode arrays (MEA).

In a second step, to resemble more accurately the fAD neuropathology, we aimed to induce tau pathology in our models, which is difficult to recapitulate in hiPSC-derived fAD models *per se*. CO organoids were infected with AAV expressing human full-length WT 2N4R tau or its pathogenic P301L variant. In the fAD CO organoids, neurons expressing P301L tau develop pathogenic tau accumulation. Using a fluorescent reporter also expressed by the AAV, we are able to observe whether fAD lineage cells are differentially affected by pathogenic tau accumulation and whether this results in differential network alterations.

The establishment of this novel human brain-like model and its deep characterisation will allow us to study the role of the inhibitory interneurons in the progression of the network imbalances observed in the patients.

POSTER 74 presented by:

NAME: Maria Escolà

Targeting nucleotide metabolism to attenuate *Pseudomonas aeruginosa* virulence

Maria Escolà[1,2], Eduard Torrents[1,2,]*

[1] Bacterial infections and antimicrobial therapies group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST). Baldiri Reixac 15-21. 08028 Barcelona, Spain.

[2] Microbiology Section, Department of Genetics, Microbiology and Statistics, Faculty of Biology, University of Barcelona, 643 Diagonal Ave., 08028, Barcelona, Spain.

Nucleotide metabolism is essential for bacterial growth and survival, supplying the necessary components for DNA replication. As a result, enzymes involved in this process are promising targets for antimicrobial strategies. In this study, we examine the role of specific nucleotide metabolism genes in the virulence and pathogenicity of *Pseudomonas aeruginosa*, a significant opportunistic pathogen linked to chronic and healthcare-associated infections.

In this study, we examined how various nucleotide metabolism-deficient mutant strains infect using the *Galleria mellonella* model. We tracked larval survival post-infection, measured bacterial load through CFU counts in hemolymph, and evaluated mutant growth under aerobic and anaerobic conditions. Additionally, we analyzed the expression of host virulence-related genes via RT-qPCR in bacteria recovered from the infected larvae.

Our findings reveal that disrupting certain nucleotide metabolism pathways greatly reduces *P. aeruginosa* virulence in vivo while maintaining bacterial viability in laboratory conditions. These results reveal a previously overlooked connection between nucleotide metabolism and pathogenicity and advocate for pursuing antimicrobial strategies focused on nucleotide metabolism. Additionally, the weakened phenotype of these mutants points to their possible use as live attenuated vaccine candidates, a topic to be examined in future research.

This study was supported by grants PID2024-158933OB-I00 funded by MCIN/AEI/10.13039/501100011033 and “ERDF A way of making Europe”; the CERCA programme and AGAUR-Generalitat de Catalunya (grant number 2021SGR01545), by the European Regional Development Fund (FEDER) and the Catalan Cystic Fibrosis association. E.T. is a researcher of the ICREA Academia 2025 program. M.E is thankful to the Generalitat de Catalunya and the European Union for their financial support through a 2025STEP00301 grant funded by the Department of Research and Universities and co-financed by the European Social Fund Plus

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 75 presented by:

NAME: Marina Rovira

Engineered Biohybrid Sphincter with Aperture Control

Marina Rovira[1], Miquel Madrid[2], Ida Kleger-Rudomin[1], Inass Himmiche[1], Elena Del Corro[2], Florencia Lezcano[1], Samuel Sánchez[1,3]

[1] Institute for Bioengineering of Catalonia (IBEC) and Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2] Catalan Institute of Nanoscience and Nanotechnology (ICN2), Barcelona, Spain
[3] Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain

Tissue-engineered skeletal muscle offers a promising platform for developing biohybrid robotic systems capable of converting the contractile activity of myofibers into functional movement. Advances in 3D bioprinting have enabled the development of engineered muscle constructs with defined geometries and spatial organization, providing new opportunities to design actuators that reproduce more complex mechanical functions. Sphincter-like structures are particularly interesting in this context, as their function relies on coordinated contraction of myofibers arranged in different orientations to regulate an opening. Reduced graphene oxide (rGO)-based microelectrodes can be used to locally stimulate engineered skeletal muscle rings, providing a way to independently activate distinct muscle regions. The aim of this study is to develop and validate a biohybrid sphincter with electrically controlled aperture using a 3D-printed skeletal muscle construct with rGO microelectrodes. With this purpose, a C2C12-based skeletal muscle sphincter was 3D-bioprinted with circularly aligned myofibers in the central region and radially aligned myofibers in the outer region; which were then matured in vitro for 14 days. The constructs were then electrically stimulated using tetanic stimulation protocols, with the electrodes positioned to selectively target different areas of the tissue. Actin staining was performed to assess myofiber orientation. After complete maturation, the bioprinted sphincter presented aligned circular myofibers in the central region and radial myofibers in the outer region, consistent with the designed architecture. Selective tetanic stimulation of the circular and radial myofiber domains successfully modulated the sphincter aperture, with distinct deformation patterns, such as closing and opening, corresponding to activation of the different areas. This work provides a foundation for developing functional biohybrid robotic systems with complex architectures and programmable actuation, opening new possibilities for advanced muscle-based robotic devices.

POSTER 76 presented by:
NAME: Marta Ardèvol Teijelo

In situ Bioprinting: 6 DOF robotic system for advanced tissue engineering. Printing directly onto curved, non-planar anatomical surfaces

Marta Ardèvol Teijelo[1,2,3], Javier Gómez Fernández[1]

[1] Bio integrated Materials and Engineering, Institute of Bioengineering of Catalonia (IBEC), Barcelona, Spain
[2] Universitat de Barcelona (UB), Spain
[3] Universitat Politècnica de Catalunya (UPC), Barcelona, Spain

What if tissue could be printed exactly where it is needed, directly onto the patient, adapting in real time to its shape?

Extrusion-based bioprinting typically relies on planar, layer-by-layer deposition onto flat substrates. The resulting constructs then need maturation, handling and surgical implantation into non-planar defects, which compromises structural integrity and geometric fidelity. *In situ* bioprinting addresses this by depositing bioinks directly at the defect site. However, handheld and cartesian 3-axis systems offer limited positional accuracy and cannot keep the nozzle correctly oriented over surfaces with variable curvature.

This work presents a six-degree-of-freedom (6-DOF) robotic platform for conformal *in situ* bioprinting of skin constructs on non-planar anatomical surfaces. The system integrates a pneumatic extrusion printhead, and a calibrated camera to the tool centre point (TCP). The acquired point cloud is reconstructed into a triangulated mesh, from which surface-conformal toolpaths are generated using local surface normals. Inverse kinematics keeps the nozzle normal to the surface at a constant *standoff* distance, and the extrusion rate is synchronised with TCP velocity. The rheological properties of the bioink (viscosity, shear-thinning behaviour and yield stress) are characterised to define the printing window and estimate shear stress at the nozzle wall. Positional accuracy and strand fidelity are quantified on planar, convex and concave substrates by 3D scanning and image analysis. Primary human dermal fibroblasts are encapsulated, and cytotoxicity is evaluated according to ISO 10993-5, alongside Live/Dead staining, metabolic activity and LDH release at days [1, 3, 7]. Full-thickness excisional wounds in *ex vivo* porcine skin provide a clinically relevant model to assess construct adhesion, shape conformity and post-printing cell viability.

The workflow is designed to provide reproducible, cell-compatible bioprinting on non-planar surfaces, validated from synthetic substrates through to a physiologically relevant skin model. The platform establishes a technical basis for point-of-care robotic biofabrication, with chronic wounds and burns as the first target applications.

Keywords: *in situ* bioprinting; robotic bioprinting; 6-DOF; point-of-care biofabrication; tissue engineering, cytotoxicity.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 77 presented by:

NAME: Michela Lain Contato

Three-dimensional spheroid model of colorectal cancer cells in different metabolic conditions

Michela Lain Contato[1,2], Jarmila Stanková[1], Sergi Casellas Diaz [1], Xavier Rovira-Clavé[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2] Department of Biomedicine, University of Barcelona, Barcelona, Spain

Cancer cells experience metabolic pressures in the tumor microenvironment, requiring metabolic adaptations that support their proliferation and survival. Through this metabolic reprogramming, cancer cells also change the available nutrient pool in their immediate neighborhood, contributing to metabolic pressures to nearby cells. However, we do not fully understand how heterogenous cell populations with different metabolic capacities interact and localize when they are exposed to diverse environments and how this affects their overall survival. In this project, we aim to investigate the ability of a pool of genetically distinct colorectal cancer cells subclones to respond to defined metabolic environments in 3D in vitro models. We first validated an in-house minimal media for cell growth supplemented with increasing concentrations of glucose, glutamine, amino acids (L-cystine and L-methionine), lactic acid, butyric acid, and fatty acids (palmitic acid and linoleic acid) to test the growth of the colorectal cancer cell line HCT116 in distinct metabolic conditions. In 2D cultures, HCT116 cells showed a variety of growth rates and phenotypes in different concentrations of metabolites. For instance, HCT116 showed limited growth once glutamine was lowered from the 2 mM physiological concentration to 0.1 mM. In parallel, using CRISR/Cas9 and an epitope-based barcoding system, we successfully knocked out 16 different metabolically relevant genes (e.g., GLUT1, IDO1, ACSL4) in duplicate to create a total of 32 HCT116 cell lines, together with 8 control cell lines. These 40 cell lines were then pooled together as a model of heterogenous tumors, grown as spheroids, and analyzed using spatial targeted proteomics to validate their growth as a complex population. Future experiments will focus on testing the growth of the pooled population of genetically distinct HCT116 subclones in the validated metabolic environments and accelerate testing through the use of a spatial barcoding system compatible with pooling hundreds of spheroids. By revealing how metabolic constraints shape subclonal growth, this system could help identify metabolic vulnerabilities that influence tumor progression and therapeutic response, providing a platform to test for potential metabolic targets against solid tumors.

POSTER 78 presented by:
NAME: Natalia Castro

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

Natalia Castro[1], Xiomara Fernández-Garibay[1], Carolina Rodríguez Gallo[1], Javier Ramón Azcón[1,2], Juan M. Fernández Costa[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Spain
[2] ICREA-Institució Catalana de Recerca i Estudis Avançats, Spain

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. The resulting decellularized ECM was digested with pepsin to solubilize the matrix and processed into a hydrogel suitable for formulation as a printable bioink. 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 | BIOMODELS AND TISSUE ENGINEERING

POSTER 79 presented by:

NAME: Nicola Manicardi

Examining How Mfsd2a-Mediated Lipid Transport Regulates BBB Endocytic Dynamics

Nicola Manicardi[1], Giuseppe Battaglia[1,2], Daniel Gonzalez-Carter[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

[2] Catalan Institution for Research and Advanced Studies (ICREA), Barcelona, Spain

The blood-brain barrier (BBB) plays a critical role in maintaining central nervous system (CNS) homeostasis, regulating neurovascular coupling, nutrient transport, and immune surveillance through specialized endothelial tight junctions and the strict suppression of non-specific vesicle trafficking. Recent findings demonstrate that BBB phenotypic specialization is fundamentally driven by unique cell-membrane protein endocytic turnover rates (ETOR), which dictates cell-surface residency time of functional membrane proteins. However, the upstream mechanisms coordinating these dynamics remain poorly understood; here, we ask how these processes are regulated at the membrane level. It is known that the transmembrane protein Mfsd2a actively suppresses non-specific endocytosis by modulating the endothelial lipid environment, specifically through the enrichment of DHA-containing phospholipids. Therefore, we aim to investigate how Mfsd2a-mediated modifications to the membrane lipid composition directly influence the cell-surface residency and the endocytic dynamics of membrane proteins to establish the molecular mechanisms by which this component cell-autonomously regulates BBB specialized phenotype and function.

To investigate Mfsd2a-mediated regulation, *in vitro* workflows are carried out using the mouse brain endothelial cell line bEnd.3 and freshly isolated primary mouse brain endothelial cells. Functional modulation of Mfsd2a expression is achieved via transient genetic knockdown of Mfsd2a using tailored small interfering RNA (siRNA) transfections. Post-silencing, Mfsd2a transport activity is functionally evaluated through an uptake assay utilizing fluorescently labelled substrate TopFluor-LPC. Downstream alterations are evaluated through measurement of overall endocytic rates of biotinylated cell-surface proteins.

Western blot analysis confirmed successful partial silencing of Mfsd2a expression in bEnd.3 cells. Functional validation through TopFluor-LPC uptake assays is currently underway to confirm the reduction of Mfsd2a transport activity upon knockdown. Following functional confirmation, general endocytic rates will be assessed to correlate Mfsd2a loss of function with alterations in global endocytosis. Together, these findings highlight a key molecular mechanism by which lipid composition controls BBB phenotypic specialization and surface protein turnover.

POSTER 80 presented by:

NAME: Oscar España Romera

Spatial features of antigen escape in a CAR-T treated murine model of melanoma

Oscar España-Romera[1,2], Sergi Casellas-Díaz[1], Xavier Rovira-Clavé[1]

[1] *Institute for Bioengineering of Catalonia, Barcelona, Spain*
[2] *University of Barcelona, Barcelona, Spain*

Chimeric antigen receptor T-cell (CAR-T) therapy has transformed the treatment of several hematological malignancies, yet its efficacy against solid tumors remains limited. A relevant mechanism leading to treatment failure is antigen escape, whereby therapeutic pressure selects tumor clones with reduced to absent expression of the targeted antigen, leading to therapy resistance and disease relapse. However, how pre-existing antigen heterogeneity drives the spatial and clonal dynamics of tumor evolution during CAR-T therapy in solid tumors remains poorly understood. In this project, we aim to combine genetic engineering and spatial proteomics to characterize subclonal evolution during antigen escape and interrogate cellular and spatial features associated with treatment resistance in a murine model of melanoma.

As an initial step, we set up a heterogeneous syngeneic murine melanoma model focused on variable cell surface expression of Tyrosinase-related protein 1 (TYRP1), a highly expressed protein in melanocytes and a promising target for CAR-T treatment. We employ B16-F10 murine melanoma cells, which can grow in mice as an immune permissive tumor, independently of TYRP1 expression as suggested by histopathological study of the tumors. We engineered a monoclonal *Tyrp1*-knockout (KO) B16-F10 cell line and reintroduced *Tyrp1* under an exogenous promoter (*Tyrp1*-OE). We sorted tumor cells by fluorescence-activated cell sorting (FACS) according to TYRP1 surface expression, and generated 15 polyclonal populations with progressively increasing TYRP1 levels. These populations were subsequently labeled using epitopebased barcoding, which is compatible with spatial proteomics readouts. We established the TYRP1 heterogeneous B16-F10 model by combining barcoded *Tyrp1*-KO cells with the 15 *Tyrp1*-OE subpopulations, generating spatially traceable tumor clones.

Current work focuses on generating primary murine CAR-T cells that target TYRP1 expressing cells. Following implantation and treatment with anti-TYRP1 CAR-T cells, we will monitor tumor evolution to characterize clonal selection and the emergence of therapy-resistant populations. Tumor tissues will be analyzed using Multiplexed Ion Beam Imaging (MIBI), enabling simultaneous detection of tumor barcodes and up to 30 phenotypic and microenvironmental markers at single-cell and spatial resolution. This will allow us to link clonal identity with tumor phenotype, spatial organization, and microenvironmental context throughout treatment.

Overall, this study will establish a spatially resolved framework to investigate subclonal antigen escape during CAR-T therapy and identify features associated with treatment resistance, providing insights for the development of more effective CAR-T strategies for solid tumors.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 81 presented by:

NAME: Palash Chandravanshi

Modelling Human Spinal Cord Injury and Repair in a 3D-Printed Organoid-on-a-Chip Device

Palash Chandravanshi[1], Dakota Coloroso[1], Marta Cuenca[2,3], Marco Fusco[1], Francisco Manuel Saez[1], Susana Rodríguez González[1], Eloi Montañez[3,4], Juan Alberto Ortega[1,2,3], Zaida Álvarez[1]

[1] *Biomaterials for Neural Regeneration Group, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain*

[2] *Department of Pathology and Experimental Therapeutics, Institute of Neurosciences, University of Barcelona, L'Hospitalet de Llobregat, Spain*

[3] *Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), L'Hospitalet de Llobregat, Spain*

[4] *Department of Physiological Sciences, Faculty of Medicine and Health Sciences, University of Barcelona, L'Hospitalet de Llobregat, Spain*

There is a critical unmet need for human-specific models of spinal cord injury (SCI), as traditional in vivo animal models suffer from poor translational success due to fundamental species differences[1], while standard in vitro systems lack the structural and functional complexity of the human central nervous system[2]. Addressing this translational gap, we report a novel, highly scalable 3D-printed spinal cord organoid-on-a-chip (SCO-on-a-chip) platform that provides a reproducible, physiologically relevant microenvironment for the long-term culture, multimodal characterization, and high-throughput therapeutic screening of human induced pluripotent stem cell (iPSC)-derived spinal cord organoids (SCOs). Device design was refined using COMSOL Multiphysics simulations to optimize fluid dynamics and minimize shear stress on the organoids, and fabrication was performed by stereolithography using a biocompatible medical-grade resin, selected after rigorous assessment of multiple materials for printability, mechanical stability a nd neural cytocompatibility. The modular platform features a glass-bottom base for real-time, high-resolution imaging and removable chambers compatible with electrophysiological recordings, and interfaces directly with an automated IH-Infinite Horizon impactor to induce controlled, reproducible mechanical contusions in geometrically confined organoids, thereby recapitulating key biomechanical features of human SCI.The optimized SCO-on-a-chip enables stable, long-term culture of up to 48 organoids within a standard six-well plate, significantly improving experimental throughput while preserving neuronal viability and architectural integrity. Following controlled mechanical impact, we successfully modelled localized injuries and quantitatively evaluated key pathological processes, including neuronal damage, inflammatory responses, and glial scar formation, validated through immunofluorescence imaging and electrophysiological analyses. Together, these features establish a robust and scalable human neurotrauma platform that combines physiological relevance with experimental throughput, providing a powerful framework for mechanistic studies, drug discovery, and the development of regenerative therapies for spinal cord injury.

References

[1]Davidsson J, Risling M. Experimental Models for Neurotrauma Research. Methods Mol Biol. 2016.

[2]Omelchenko A, Singh NK, Firestein BL. Current advances in in vitro models of central nervous system trauma. Curr Opin Biomed Eng. 2020.

Acknowledgements

We gratefully acknowledge funding from the "la Caixa" Foundation (La Caixa Health: SPINAL-TraHumanoid, project code LCF/PR/HR25/52450044); an FPI fellowship (Grant PRE2022-101803) and Grant RYC2020-028732-I, both funded by MICIU/AEI/10.13039/501100011033 (the latter co-funded by "ESF Investing in your future"); and an IRP Research Grant (contract number P199).

POSTER 82 presented by:

NAME: Paulina Teresa Sobierajska

Role of Amorphicity in Determining the Structure, Morphology, Thermal Stability and *In Vitro* Biological Response of Calcium Phosphates

Paulina Sobierajska[1,2], Nataliia D. Pinchuk[1,3], Ariadna Pielok[1,4], Katarzyna Wiglusz[5], Vasyl Kinzhybalo[1], Oleksii Bezkrovny[1] and Rafal J. WIGLUSZ[1]

[1] Division of Biomedical Physicochemistry, Institute of Low Temperature and Structure Research, Polish Academy of Sciences, Wroclaw, Poland

[2] Biomaterials for Regenerative Therapies Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain

[3] Frantsevich Institute for Problems of Materials Science of the NAS of Ukraine, Pritsaka, Kyiv, Ukrain

[4] Laboratory of Preclinical Research and Cell Transplantation "In VetBio",Department of Pharmacology and Toxicology, Faculty of Veterinary Medicine, Wroclaw University of Environmental and Life Sciences, Wroclaw, Poland

[5] Department of Basic Chemical Sciences, Faculty of Pharmacy, Wroclaw Medical University, Wroclaw, Poland

Calcium phosphates occur in both amorphous and crystalline forms. Amorphous calcium phosphates (ACPs) may transform into more stable crystalline phases, including hydroxyapatite and tricalcium phosphate [1]. In this work, nanosized ACP powders were synthesized by rapid precipitation and dried either by freeze-drying (ACP-L) or oven drying (CP-D). The influence of the drying method on phase evolution, morphology, and thermal stability was investigated using XRPD, HRTEM, TGA, and DSC. Significant differences in crystallinity, thermal behaviour, and particle morphology were observed between the two materials. Preliminary biological studies demonstrated distinct cytotoxicity profiles, cell-material interactions, and effects on MG-63 cell morphology and gene expression.

References

[1] C. Combes, C. Rey, "Amorphous calcium phosphates: Synthesis, properties and uses in biomaterials", Acta Biomater 6, 3362–3378, 2010

Acknowledgements

The Bekker Programme (BPN/BEK/2025/1/00316) of the Polish National Agency for Academic Exchange (NAWA) is gratefully acknowledged.

POSTER 83 presented by:
NAME: Petra Bauzon

Linking sarcolemmal instability to metabolic dysregulation: a DMD-on-Chip Platform investigating mitochondrial dysfunctions

Petra Bauzon[1], Ainoa Tejedera Villafranca[1], Juan M. Fernández Costa[1], Javier Ramón Azcón[1,2]

[1] Biosensors for Bioengineering group, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain;
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.

Duchenne muscular dystrophy (DMD), caused by dystrophin deficiency, has been traditionally viewed as a structural disorder. However, it is increasingly recognized as having a critical metabolic component driven by mitochondrial dysfunction. Mitochondrial impairment is emerging to be a central contributor to energy deficits, calcium dysregulation, and progressive muscle degeneration observed in DMD.

Consequently, targeting metabolic pathways through therapies aimed at restoring mitochondrial function has emerged as a promising strategy to complement existing treatments. However, current models (e.g., 2D cell cultures, animal studies) often fail to adequately recapitulate human pathophysiology, hindering the acquisition of mechanistic insights and the validation of therapeutic approaches.

To address this problem, this project will focus on the development of a skeletal muscle Organ-on-Chip platform with integrated plasmonic biosensors to model and investigate DMD-associated mitochondrial dysfunction and evaluate possible metabolic therapies. This system will combine 3D skeletal muscle models and biosensor technologies, advancing bioengineered systems through several innovations. Firstly, patient-derived cell-based disease models allow to replicate human pathophysiology and assess metabolic responses to therapeutic candidates. In particular, the possibility of inducing sarcolemmal damage by eccentrical contraction of the bioengineered skeletal muscle tissue models will enable to assess the causal relationship between sarcolemmal instability and mitochondrial impairment. Secondly, integrated biosensors enable real-time label-free monitoring of metabolic markers. Finally, the microfluidic integration of these technologies into an OoC platform will enable synchronized tissue culture and dynamic biosensing of relevant biomarkers in engineered skeletal muscle.

The platform's capacity for dynamic biosensing during physiologically relevant mechanical stress establishes a mechanistic link between sarcolemmal instability and metabolic collapse while enabling high-throughput evaluation of mitochondrial enhancers, appealing candidates in combinatorial strategies for DMD treatment. By bridging human-relevant tissue models with continuous biomarker monitoring, this technology provides a translational tool for precision DMD therapy development and personalized treatment stratification.

POSTER 84 presented by:
NAME: Pol Picón Pagès

Structural and Mechanistic Insights into GPR133 Signaling in Glioblastoma Multiforme

Pol Picón-Pagès[1,2,3,4], Marc Riu[1,2,3,4], Tamara Brkić[1,2,3,4], Mohammad Azan[1,2,3,4], Elena de Cecco[5], Adriano Aguzzi[5], José Antonio del Río[1,2,3,4]

[1] Molecular and Cellular Neurobiotechnology, Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Science Park of Barcelona, Barcelona, Spain.
[2] Department of Cell Biology, Physiology and Immunology, Faculty of Biology. University of Barcelona, Barcelona, Spain.
[3] Ciberned (Network Centre of Biomedical Research of Neurodegenerative Diseases), Institute of Health Carlos III, Spain.
[4] Institute of Neuroscience, University of Barcelona, Barcelona, Spain
[5] Institute for the Science of the Aging Brain (ISAB), Gallen, Switzerland.

Glioblastoma multiforme (GBM), also known by World Health Organization as 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 cell adhesion towards surfaces and other GPR133 cells, triggering an induction of mechanotransduction, by focal adhesion kinase (FAK) phosphorylation, altered tubulin expression levels, and a shift in Yes-associated protein (YAP) nuclear relocalization. This increased intercellular adhesion, in turn, paradoxically, reduces cellular migration and invasiveness. Therefore, suggesting expression of GPR133 to have a fundamental role as a structural protein for the whole tumor, enabling external tumoral cells division and invasion. In conclusion, we present the first known model of native GPR133 overexpression in GBM cells. With this model we have demonstrated the putative mechanistic role of GPR133 in tumor development, which aims to contribute to the development of novel therapeutic strategies targeting this lethal disease.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 85 presented by:

NAME: Rita Grimalt Mirada

A Microengineered Platform for the Generation of Single-Lumen Human Spinal Cord Organoids

Grimalt-Mirada R[1], Barceló X[1], Sáez FM[1], Ortega JA[2,3], Álvarez Z[1,4,5]

[1] Biomaterials for Neural Regeneration, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain;
[2] Department of Pathology and Experimental Therapeutics, Institute of Neurosciences, University of Barcelona, L'Hospitalet de Llobregat, Spain
[3] Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), L'Hospitalet de Llobregat, Spain
[4] CIBER en Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Madrid, Spain
[5] Center for Regenerative Medicine (CRN), Northwestern University, Chicago, USA.

Human spinal cord organoids (hSCOs) are powerful models to study early neurodevelopment and disease in a human-specific context. However, their intrinsic stochastic organization often gives rise to multiple neural tube-like structures instead of a single polarized neuroepithelial tube (**Fig1A**). We present a high-resolution microengineered platform that guides the self-assembly of human induced pluripotent stem cells (hiPSCs) into single lumen hSCOs with improved structural organization and dorsoventral patterning reminiscent of the early neural tube (**Fig1B**).

2-Photon Polymerization (2PP) 3D printing was used to fabricate arrays of microwells with a central pillar, around which hiPSCs self-assembled into toroidal structures. Toroids were differentiated toward spinal cord neural lineage following a standard hSCO protocol and the spatial arrangement of different neural cell subtypes was evaluated by immunocytochemistry. Post-fabrication characterization confirmed the high resolution of the 2PP-printed microscale features. The platform supported the formation of continuous 3D cellular toroids surrounding the central pillar, which developed into tube-like structures that overgrew the pillar after 12 days *in vitro*. The resulting tubular structures displayed a defined lumen and expressed key markers of neural induction, including SOX2, TUJ1, and Ki67. Furthermore, early development markers FOXA2 and NKX2.2 showed localized expression consistent with dorsoventral polarization.

We propose a microfabrication strategy to promote single-lumen organization reminiscent of early neural tube development in hSCOs. This shift from conventional organoid self-aggregation to geometry-guided morphogenesis represents a key step toward generating biomimetic hSCOs with improved structural fidelity. Ultimately, this system provides a promising platform for studying human spinal cord development and, ultimately, injury and regeneration.

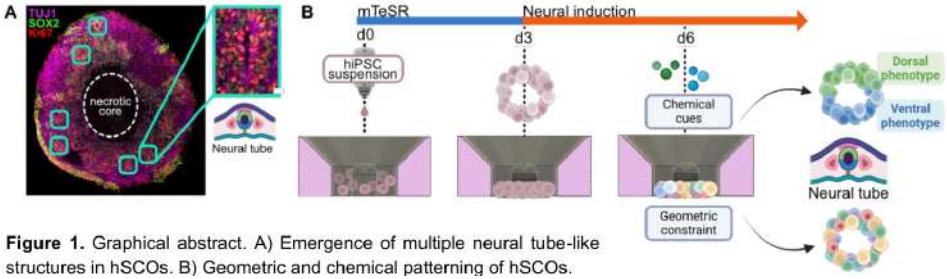


Figure 1. Graphical abstract. A) Emergence of multiple neural tube-like structures in hSCOs. B) Geometric and chemical patterning of hSCOs.

Acknowledgements: This project was funded by the fellowship 2025 STEP 00182 from Generalitat de Catalunya and the European Union, HR25-00406 (Z.A) from CaixaHealth, La Caixa Foundation, as well as by the European Union (ERC, 101230979 - SpineCraft). J.A.O. and Z. A. are currently Ramon y Cajal Investigators.

POSTER 86 presented by:
NAME: Thomas Wilson

Epifluidics: a scaffold-free platform for perfusable, geometrically programmable, epithelial tubes

Thomas Wilson [1 2], Nimesh Chahare [1 3], Özge Özguç [1], Tom Golde [1], Xavier Trepat [1 2 4 5]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Barcelona, Spain.
[2] Facultat de Medicina, Universitat de Barcelona, Barcelona, Spain.
[3] LaCàN, Universitat Politècnica de Catalunya- BarcelonaTech, Barcelona, Spain.
[4] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.
[5] Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina, Barcelona, Spain.

Tubular epithelia, such as the vasculature, the intestinal and renal tubules, and the bile ducts, develop and function under a combination of imposed geometry and flow-derived shear that is almost impossible to decouple in vivo. Existing platforms struggle to combine independent control of tube geometry and luminal flow with high-resolution imaging of a scaffold-free tissue surface. Here we introduce Epifluidics, a platform for generating suspended, semi-cylindrical epithelial tubes bonded to a planar, protein-patterned PDMS substrate and connected to an underlying pressure channel via inlet and outlet holes. Tubes form by seeding a confluent monolayer over a sacrificial collagen matrix filling the substrate apertures; enzymatic removal of the matrix leaves suspended monolayers over the holes, and substrate-patterned fibronectin guides their spontaneous, ion-pumping-driven delamination. Applied pressure then coalesces these structures into a continuous, perfusable channel. The resulting tube footprint closely follows the imposed substrate pattern, luminal cross-sectional area and strain scale with applied pressure, and particle tracking reveals a unidirectional, near-parabolic velocity profile consistent with laminar, pressure-driven flow. As a proof of concept for tissue-driven actuation, we show that the optogenetic tools OptoShroom3 and OptoGEF-RhoA can be incorporated without compromising tube formation, and that localized blue-light illumination reproducibly drives global changes in tube geometry. Together, these results establish Epifluidics as a quantitatively characterised, geometrically programmable, and self-actuating platform for tubular epithelia.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 87 presented by:

NAME: Timothée Caboche

A Magnetic Actuator-Based Platform for Functional Assessment of 3D Human Skeletal Muscle Bioengineered Tissues in Myotonic Dystrophy

Timothée Caboche[1], Carolina Rodríguez-Gallo[1], Chiara Ninfali[1], Javier Ramón-Azcón[1,2], Juan M. Fernández-Costa[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Spain;
[2] ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain

Myotonic dystrophy type 1 (DM1) is the most common muscular dystrophy and is characterized by multisystemic symptoms such as myotonia, muscle weakness or cardiac muscle dysfunction. No treatment options are currently available. In this context, threedimensional (3D) tissue has emerged as a relevant approach to develop more relevant biological models compared to traditional 2D cultures. It has previously been demonstrated that controlling the cellular microenvironment can enhance tissue morphogenesis, cell differentiation, and functionality. In our laboratory, we have developed a contractile DM1 3D skeletal muscle tissues model using immortalized myoblasts derived from DM1 patients encapsulated in biomaterials, attached between two flexible, biocompatible pillars. This model is combined with an electrical pulse stimulation (EPS) platform (MyoMoves) to reproduce muscle contraction and to quantify the musclegenerated force by measuring pillar displacement. These models recapitulate DM1 phenotypes *in vitro*, including muscle myotonia and CLCN1 splicing abnormalities.

In this project, we aim to develop a magnetic actuator-baseds platform that can reproduce DM1 phenotypes and induce percussive myopathy, complementing the existing MyoMoves approach. To achieve this, we are designing chips with flexible pillars with magnetic nanoparticles to support 3D tissues. By aligning the magnetic moments of these particles, we can induce pillar bending through magnetic torque in response to an external magnetic field. To generate this deflection, we aim to develop a magnetic actuation system based on electromagnets compatible with 24-well plate used for cell culture, which we employ in our 3D encapsulation process.

By varying magnetic field strength, the applied torque can be controlled to define stretching regimes. This system provides a controlled mechanical environment to investigate the effects of mechanical loading on muscle differentiation, gene expression, and muscle fiber-type specification.

This platform will enable deeper investigation of DM1 pathophysiology and can be readily extended to cardiac tissue models and high-content drug screening applications.

POSTER 88 presented by:

NAME: Tobias Walther

DNA hydrogel microparticles as phantom cells for tissue engineering

Tobias Walther[1,2], Cassian Afting[3], Eleni Dalaka[1], Gotthold V. Fläschner[1], Simon Brauburger[4], Bastian K. Kraus[4], Manuel Gomez-Gonzalez[1], Oliver M. Drozdowski[4], Pere Roca-Cusachs[1], Ulrich S. Schwarz[4], Joachim Wittbrodt[3], Xavier Trepat[1], Kerstin Göpfrich[2]

[1] *Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain*
[2] *Institute for Molecular Biology of Heidelberg University (ZMBH), Heidelberg, Germany*
[3] *Centre for Organismal Studies (COS), Heidelberg, Germany*
[4] *Institute for Theoretical Physics, Heidelberg, Germany*

Hydrogel microparticles (HMPs) are powerful tools for the study and manipulation of 3D cellular systems. Engineered to allow physical interactions with living cells and chemical signalling through external triggers, they can be directly interfaced with growing tissues and act as functional cell mimics: phantom cells. Most polymeric HMPs, however, lack versatility in terms of their capacity for targeted chemical functionalization combined with fine-scale mechanical programmability, limiting their complexity. DNA-based materials offer promising properties in this regard due to their sequence-defined self-assembly, precise mechanical tuning, and straightforward chemical modification. Here, we introduce fully DNA-based hydrogel microparticles (DNA-HMPs) as a new class of multifunctional phantom cells for tissue engineering. DNA-HMP size can be controlled via microfluidics to span the size range of human tissue cells. Making use of DNA sequence design, DNA-HMPs demonstrate finely programmable mechanics with viscoelastic behaviour and Young's Moduli between 30 Pa – 6 kPa, as validated by real-time deformability cytometry and indentation. This way, their mechanical properties can be tailored to mimic specific cell types of target tissues. DNA-HMP modification based on click chemistry further enables controlled physical interactions with living cells for force sensing in 3D, as well as binding of morphogenic compounds. Through light-based stimuli-response, these morphogens can be released from the DNA-HMPs to spatiotemporally control stem cell differentiation in organoids, increasing cell type diversity. Combining programmable material properties with straightforward functionalization and stimuli-responsiveness, DNA-HMPs represent a versatile new tool to probe and manipulate tissue behaviour in 3D cell culture, advancing tissue engineering through DNA nanotechnology.

POSTER | BIOMODELS AND TISSUE ENGINEERING

POSTER 89 presented by:

NAME: Vicent Ribas Serra

Sex- and model-dependent hepatic pyruvate flux alterations in obesity revealed by HP-^{13}C NMR

Vicent Ribas[1], Jakub Podraza[1], Giovanni Vito Spinelli[1], David Gómez-Cabeza[1], Alba Herrero-Gómez[1], Helena Marí de Nova[2,3], Joan-Marc Servitja[2,3], Irene Marco-Rius[1]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

[2] Pathogenesis and Prevention of Diabetes Group, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

[3] Centro de Investigación Biomédica en Red de Diabetes y Enfermedades Metabólicas Asociadas (CIBERDEM), Madrid, Spain

Obesity induces sex- and model-dependent metabolic alterations, but how diet-induced (high-fat diet, HFD) and genetic (Ob/Ob) obesity differentially affect hepatic pyruvate handling remains unclear. Hyperpolarized [1-^{13}C]pyruvate NMR enables real-time, noninvasive assessment of hepatic metabolic fluxes, offering unique insight into sex- and model-dependent alterations in hepatic pyruvate flux.

Male and female C57BL/6J mice were studied under two obesity experimental approaches: 20-week high-fat diet feeding or leptin-deficient Ob/Ob genotype, compared with regular diet controls. All animals underwent metabolic phenotyping, liver fat quantification by MRI–Proton Density Fat Fraction (MRI-PDFF), and HP-^{13}C NMR to quantify alanine, lactate and bicarbonate production, kinetic rate constants and pyruvate intracellular transport.

At endpoint, both HFD and Ob/Ob mice of both sexes showed increased body weight, visceral adiposity, fasting hyperglycaemia and insulin resistance, with HFD-induced insulin resistance being more pronounced in males. Liver histology, triglycerides and MRI-PDFF confirmed marked steatosis in both models, with model- and sex-dependent differences in lipid distribution.

HP-[1-^{13}C]pyruvate NMR highlighted pronounced metabolic distinctions between the two obesity models. In Ob/Ob mice, alanine production rose specifically in males, while both sexes showed changes in *kp(ala)* and *kp(lac)*. These animals also displayed higher pyruvate intracellular transport rate (*kO_in*) and were the only group with detectable bicarbonate, consistent with increased mitochondrial pyruvate oxidation. Conversely, HFD mice exhibited only modest, sex-dependent adjustments and no bicarbonate signal, indicating a far less extensive remodelling of hepatic pyruvate metabolism.

HP-[1-^{13}C]pyruvate NMR, combined with MRI-PDFF, provides a sensitive and non-invasive means to characterise obesity-related hepatic metabolic reprogramming beyond conventional tests. By resolving alanine, lactate, bicarbonate and transport kinetics across HFD and Ob/Ob models and between sexes, this approach provides a real-time readout to detect and mechanistically stratify metabolic liver disease in vivo.

POSTER 90 presented by:

NAME: Xavier Barceló

Placenta-Derived ECM as a Spinal Cord-Mimetic Biomaterial

X. Barceló[1], E. Garrido[1], F. M. Sáez[1], O. Castaño[2], J. A. Ortega[3,4], Z. Álvarez[1,5,6]

[1] Biomaterials for Neural Regeneration Group, Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain

[2] Electronic and Biomedical Engineering Department, University of Barcelona, Barcelona, Spain;

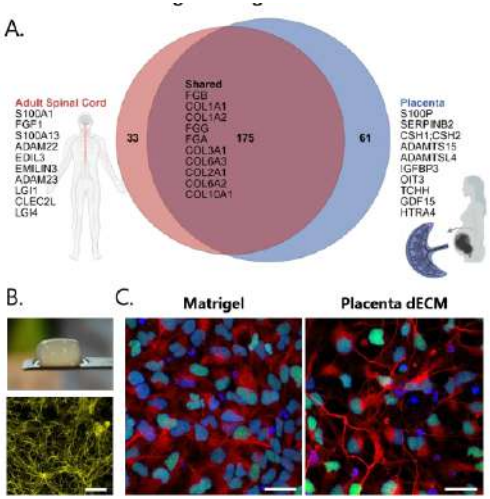
3 4 Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), L'Hospitalet del Llobregat, Spain; Department of Pathology and Experimental

Therapeutics, Institute of Neurosciences, University of Barcelona, L'Hospitalet de Llobregat, Spain

[5] CIBER en Bioingeniería, Biomateriales y Nanomedicina, CIBER-BBN, Madrid, Spain

[6] Center for Regenerative Medicine (CRN), Northwestern University, Chicago, USA

Recapitulating the spinal cord matrisome, which actively regulates cell behaviour, is critical for physiologically relevant models and, potentially, for the development of regenerative therapies. In this context, decellularized extracellular matrix (dECM)-derived biomaterials excel by retaining tissue-specific proteins. Here, human placenta serves as an abundant and ethically sourced biomaterial with over 84% of the adult spinal cord matrisome composition found in the placenta matrisome (**Figure 1A**). Its composition is rich in glycoproteins, including different types of laminins and fibronectins, as well as abundant structural collagens. When analyzed through Gene Ontology enrichment terms, its composition heavily clusters around pathways critical for tissue regeneration and organization, such as response to wounding, cell adhesion, and vasculature development, making it an ideal bioinstructive platform for spinal cord tissue engineering.



After successful decellularization (< 50 ng of DNA/mg dW), the placenta dECM retains key components, including laminins, fibronectin, and collagens, providing a biologically relevant microenvironment (**Figure 1B**). The biocompatibility of this biomaterial was assessed using neural progenitor cells, demonstrating a cell survival rate of over 90%. Furthermore, culturing these progenitors on dECM-coated surfaces induced the development of an extensive neurite network with a 6.5-fold increase in maximum neurite elongation compared to standard Matrigel (**Figure 1C**). Because a robust vascular network is crucial for spinal cord function, we evaluated the vascular capacity of the dECM by using it as an embedding matrix for vascular organoids.

Compared to standard Matrigel, placenta ***Figure 1.*** A. Venn diagram showing the overlap dECM supported comparable vascular *between the adult spinal cord and the placenta* organoid growth while inducing a 6.8-fold *matrisomes; B. Top – Placenta dECM hydrogel,* increase in the Iba1-positive population. This *Bottom – Staining for Collagen IV within the placenta*indicates that placenta dECM not only *derived matrix. C. Neural progenitor cells grown on* supports the 3D embedding and growth of *either Matrigel or placenta dECM (red = TUJ1, green* vascular organoids but also significantly *= SOX2, blue = DAPI); Scale bars are equal to 20* µ*m* enriches the Iba1-positive cell population. *respectively*.

Finally, we evaluated the potential of incorporating motor neurons, a key component of spinal cord functionality, within the placenta dECM. To achieve this, we seeded GFP-labeled human motor neurons within highly accurate spinal cord exoskeletons that recapitulate the macroscopic organization and size (~1 cm in diameter) of the human spinal cord. Already after 7 days in culture, these motor neurons were able to extend their neurites.

In summary, human placenta dECM serves as a powerful spinal-cord-mimetic biomaterial capable of providing a bioinstructive microenvironment for both neural and vascular populations. The described biomaterial offers a promising tool for developing advanced, biomimetic models of the human central nervous system.

FLASH presented by:

NAME: Daniel Moya Rull

A reproducible and scalable human airway and lung organoid platform for infection modelling and therapeutic screening

Daniel Moya-Rull[1], Maria Morera Trullas[1], Máiréid Bull[2], Ria Lassaunière[2], Elena Garreta[1], Nuria Montserrat[1]

[1] Pluripotency for organ regeneration (PR Lab), Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.

[2] Virus Research and Development Laboratory, Virus & Microbiological Special Diagnostics, Statens Serum Institut, Copenhagen, Denmark.

Human induced pluripotent stem cell (hiPSC)-derived lung and airway organoids have emerged as powerful tools to study respiratory development, infection, and disease in a controlled and human-relevant setting. In this work, we developed an innovative scalable free-floating culture system that reduces the reliance on organoid matrigel embedding without compromising organoid differentiation. hiPSC-derived lung progenitor cells were efficiently generated through a stepwise differentiation protocol, starting with the induction of primitive streak and definitive endoderm commitment, followed by progression through the anterior foregut endoderm stage, ultimately yielding lung progenitors characterized by the expression of the transcription factor NKX2-1 on day 14 of differentiation. Day 14 lung progenitors were then used for the scalable production of both proximal airway epithelial organoids and distal lung organoids through exposure to specific proximal-distal lung inductive signals until day 26 of differentiation. By culturing the organoids under agitation and optimized culture media conditions, we achieved consistent and robust organoid development, scaling the system to more than 1,000 organoids per experiment and substantially increasing experimental throughput. Histological analysis of airway epithelial and lung organoids showed characteristic maturity-associated morphological features including pseudostratified epithelial structures and alveolar-like structures. Immunofluorescence and qPCR analyses confirmed the identity and cellular composition of both lung and airway epithelial organoids, expressing markers of club cells, globet cells, and ciliated cells. Furthermore, to evaluate their suitability as preclinical platforms for modelling host responses to viral infection, human airway epithelial and lung organoids were challenged with six SARS-CoV-2 variants. Mock and infected organoids were collected 72 hours post-infection and analyzed by immunofluorescence and confocal microscopy, followed by quantitative image analysis to determine the extent of viral infection and assess variant-specific infectivity in both airway and lung organoids. Together, these findings establish a robust, scalable, and reproducible human airway and lung organoid platform suitable for infection modeling and future therapeutic screening in a preclinical context.

FLASH PRESENTATION | MECHANOBIOLOGY

FLASH 91 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], Miguel González-Martín[1 2], Gotthold Fläschner[1], Roger Pons[3], Sílvia Pujals[4], Felix Campelo[5], María F. García-Parajo[3 6], Amy E.M. Beedle[7], Pere Roca-Cusachs[1 2]

[1] *Institute for Bioengineering of Catalonia (IBEC), 08028 Barcelona, Spain.*
[2] *Facultat de Medicina, Universitat de Barcelona, 08028 Barcelona, Spain.*
[3] *The Institute of Photonic Sciences (ICFO), 08860 Barcelona, Spain.*
[4] *Institute for Advanced Chemistry of Catalonia (IQAC), 08034 Barcelona, Spain.*
[5] *Facultat de Medicina i Ciències de la Vida, Universitat Pompeu Fabra, 08003 Barcelona, Spain.*
[6] *Institució Catalana de Recerca i Estudis Avançats (ICREA), 08010 Barcelona, Spain.*
[7] *Department of Physics, King's College London, London WC2R 2LS, UK.*

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.

FLASH 92 presented by:
NAME: Laura Parra Gutiérrez

Characterization of matrix invasion and monolayer formation during early mouse embryo implantation

Laura Parra[1], Amélie L. Godeau[1], Júlia Fabà-Costa[1], Marc Casals[1], Anna Seriola[1], Samuel Ojosnegros[1]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), 08028 Barcelona, Spain.

Embryo implantation is a crucial step in mammalian reproduction, where mechanical forces and cell contractility play a fundamental role. However, due to the inaccessibility of the implantation event *in vivo*, the role of these mechanical forces in implantation remains poorly understood. To overcome this limitation, we use an *in vitro* setup mimicking the physiological conditions of the endometrium to study mouse embryo implantation. In contrast to previous studies, we focus on embryos at early stages of implantation, shortly after attachment to the collagen matrix, allowing us to investigate the mechanics of the implantation process. We characterize the competition between monolayer formation on the surface and matrix invasion, as well as the associated collagen remodeling and displacement. We observe that matrix invasion and monolayer formation do not occur at a constant rate. Instead, embryos modulate their implantation dynamics, which results in a general initial phase dominated by invasion and a subsequent phase where invasion speed decreases and monolayer expansion becomes dominant. Remodeling of the collagen generates axes of preferential deformation, which are generally maintained over time and align with directions of maximal monolayer expansion. Reduction of contractile forces through the inhibition of myosin activity resulted in a diminishing of monolayer expansion, matrix invasion and deformation of the collagen. The formation of preferential deformation axes was disrupted, resulting in an isotropic deformation field around the embryo and abolishing alignment with monolayer expansion direction. Future work will focus on the feedback mechanism between traction force and the resulting matrix stiffening and its impact on embryo implantation.

POSTER | MECHANOBIOLOGY

POSTER 93 presented by:

NAME: Àlex Jiménez Becerra

The Effect of Nematic Defects on the Curvature of 3D Cellular Tissues

Àlex Jiménez-Becerra[1,2], Pau Guillamat[3], Juan F. Abenza[1,4], Marino Arroyo[5,6], Xavier Trepat[1,2,4,7]

[1] *Institute for Bioengineering of Catalonia, The Barcelona Institute for Science and Technology, Barcelona, Spain*
[2] *Facultat de Medicina, Universitat de Barcelona, Barcelona, Spain*
[3] *Facultat de Química, Universitat de Barcelona, Barcelona, Spain*
[4] *Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Barcelona, Spain*
[5] *LaCàN, Universitat Politècnica de Catalunya (UPC)–BarcelonaTech, Barcelona, Spain*
[6] *Centre Internacional de Mètodes Numèrics en Enginyeria (CIMNE), Barcelona, Spain*
[7] *Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain*

Nematic alignment of elongated cells in tissues plays a significant role in a wide range of biological processes and cellular behaviors (1). In particular, tissue morphogenesis has recently been linked to the presence of nematic defects in the underlying cellular organization (2). In this work, we use a custom micropatterning technique on soft gels to control cell alignment and introduce well-defined nematic defects in fibroblast monolayers. Besides, we combine single-cell imaging, tracking and quantitative analysis tools to characterize both the patterned monolayers and the more complex shapes they form upon detachment from the substrate. Thus, by relating orientational order in two dimensions to geometry and curvature of three-dimensional structures, we aim to better understand the mechanisms linking cellular organization and curvature tissue-scale morphogenesis.

1 A. Doostmohammadi, B. Ladoux, Physics of liquid crystals in cell biology. *Trends in Cell Biology*, **32**, 140-150 (2021).

2 P. Guillamat *et al.*, Guidance of cellular nematic elastomers into shape-programmable living surfaces. *Science,* **392**, 317-323 (2026).

POSTER 94 presented by:
NAME: Alice Perucca

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

Alice Perucca [1], Janet van der Graaf Mas [1], Pau Guillamat [1], Ana Henriques [2], Eduard Batlle [2,3,4], Xavier Trepat [1,3,5,6].

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain.
[2] Institute for Research in Biomedicine (IRB), Barcelona, Spain.
[3] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.
[4] Centro de Investigación Biomédica en Red en Cáncer (CIBERONC), Barcelona, Spain.
[5] Unitat de Biofisica i Bioenginyeria, Facultat de Medicina, Universitat de Barcelona, Barcelona, Spain.
[6] Center for Networked Biomedical Research on Bioengineering, Biomaterials and Nanomedicine (CIBERBBN), 08028 Barcelona, Spain.

The tumour microenvironment (TME) is a complex system in which cancer cells, immune cells, cancer-associated fibroblasts (CAFs), and the extracellular matrix (ECM) interact to regulate tumour progression. A prominent feature of the TME is the alignment of ECM fibers, particularly fibronectin, which can exhibit nematic order, the collective alignment of elongated structures. Local disruptions in this organization, known as nematic defects, have been associated with distinct mechanical properties and have been observed near tumour–stroma interfaces in several tumour types. CAFs can also adopt similar patterns of alignment and defect organization, suggesting that cellular and ECM architecture may jointly influence the physical properties of the tumour microenvironment. These structural features may have important consequences for immune-cell infiltration. Although T cells can migrate along aligned ECM structures, dense and highly organized matrices can also restrict their access to tumour tissue. However, the extent to which nematic organization and defects influence T-cell migration remains poorly understood.

Here, we use a controlled *in vitro* system of fibroblast monolayers cultured on polyacrylamide gels to investigate how the organization of fibroblast networks affects T-cell behaviour. Specifically, we compare T-cell migration through aligned and disordered fibroblast networks and examine whether nematic defects act as physical cues or barriers to T-cell movement. By linking fibroblast organization and its mechanical features to immune-cell migration, this work aims to determine whether nematic architecture contributes to immune exclusion and to provide insight into how physical organization within the TME regulates immune access.

POSTER | MECHANOBIOLOGY

POSTER 95 presented by:

NAME: Amélie Godeau

Mechanics of Human Embryo Implantation

Amélie Luise Godeau[1], Laura Parra[1], Julia Faba Costa[1], David Bohringer[2], Ot Massafret[1], Marc Casals[1], Anna Ferrer-Vaquer[1], Miquel Solé[3], Montse Boada[3], Ben Fabry[2], Anna Seriola[1], Samuel Ojosnegros[1]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), 08028 Barcelona, Spain.

[2] Department of Physics, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany

[3] Reproductive Medicine Unit, Department of Obstetrics, Gynaecology and Reproduction, Dexeus Mujer, Hospital Universitari Dexeus, Gran Vía Carles III, 71-75, 08028, Barcelona, Spain

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 cytotrophoblast and syncytiotrophoblast. 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 exhibited characteristic interstitial implantation, progressively embedding within the extracellular matrix while actively remodeling their surroundings and generating traction forces. Matrix displacement was predominantly radial and increased over time, whereas transverse displacement displayed bidirectional dynamics, with both positive and negative displacement. Matrix penetration was preceded by a transient increase in actin intensity, followed by sustained actin enrichment during invasion, suggesting that cytoskeletal activation accompanies the onset and progression of embryo penetration. Inhibition of matrix metalloproteases reduced matrix penetration and shifted the transverse displacement pattern towards negative displacement, providing functional evidence that extracellular matrix degradation contributes to the mechanical remodeling required for embryo invasion.

Together, these findings establish human embryo implantation as a mechanically active process in which actin-dependent force generation and extracellular matrix degradation act together to drive remodeling and penetration of the matrix.

POSTER 96 presented by:

NAME: Anabel-Lise Le Roux

Acute Cell Stretching Triggers a Rapid Intrinsic Decrease in Plasma Membrane Bilayer Tension

Anabel-Lise Le Roux[1], Joaquim Torra[2], Evelyn Coderch[1], Nimesh Chahare[4], Xavier Trepat[1,3,5], Felix Campelo[2,6], María Garcia-Parajo[2], Pere Roca-Cusachs[1,3]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Technology (BIST), Barcelona, Spain.
[2] ICFO-Institut de Ciencies Fotoniques, The Barcelona Institute of Science and Technology, Barcelona, Spain.
[3] University of Barcelona, Barcelona, Spain.
[4] European Molecular Biology Laboratory (EMBL), Barcelona, Spain.
[5] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.
[6] Department of Medicine and Life Sciences (MELIS), Universitat Pompeu Fabra (UPF), Barcelona, Spain

Mechanical stretch is a ubiquitous physiological stimulus that drives key cellular adaptations during breathing, cardiovascular pulsing, and tissue homeostasis. The plasma membrane (PM) is central to this process; it acts as a primary mechanosensor that triggers downstream mechanosignaling pathways while simultaneously protecting cell integrity and governing material exchange. Gaining an exhaustive understanding of cell homeostasis requires exploring how the PM handles these stretching forces. However, dissecting the membrane's tensional response to physical strain remains a major biophysical challenge because tension builds from interconnected components, including at least the lipid bilayer, osmotic state, membrane-to-cortex attachments (MCA) and the cortex itself. Consequently, conventional techniques typically measure a convoluted "apparent" tension, making it difficult to isolate the bilayer component itself. Furthermore, while osmotic shock responses are frequently used to study tension shifts, how physical stretch specifically regulates the lipid bilayer remains poorly understood, despite its vast physiological relevance. To resolve this, we combined a fluorescent membrane tension probe (Flipper-TR) with fluorescence lifetime imaging microscopy (FLIM) to selectively isolate bilayer tension. We integrated this approach with a unique microfluidic stretching device (patent EP25383565.6) engineered for high-magnification, high optical quality, real-time imaging of the highly extended basal membrane during strain application. Surprisingly, acute cell stretching triggered a large, sustained decrease in PM bilayer tension. This counterintuitive response was independent of both PM phase separation (cholesterol availability) and branched actin polymerization, revealing a rapid, intrinsic PM relaxation mechanism that prevents extreme tension fluctuations during sudden tissue deformation. Moving forward, we aim to further decouple these biophysical components by probing how other classical cytoskeletal drugs, as well as disruption of MCAs, modulate this stretch-induced relaxation. Ultimately, our findings demonstrate that distinct mechanical stimuli trigger fundamentally different membrane responses with unique homeostatic and mechanosignaling consequences, while validating a powerful technological platform for high-resolution biophysical imaging during active mechanical deformation.

POSTER | MECHANOBIOLOGY

POSTER 97 presented by:

NAME: Annalisa Calò

Study of Neuromelanin (NM) accumulation in neurons through AFM micro and nanomechanics

Beatriz Cantero Nieto[1,2], Mauricio Cano Galván[1,2], Gabriel Gomila[1,2] and Annalisa Calò[1,2]

[1] Institute for Bioengineering of Catalonia, c/ Baldiri i Reixac 11-15, 08028, Barcelona, Spain.

[2] Department of Electronic, Biomedical and Telecommunication Engineering, Physics Faculty of the University of Barcelona, C/ Martí i Franquès 1, 08028, Barcelona, Spain

Diseases like cancer and cardiovascular diseases are characterized by transformations at the cellular level which directly impact on the expression of protein fibers that form the cell cytoskeleton. For this reason, changes in cell mechanics are often accompanied by these biomolecular transformations and can be detected by highly sensitive local techniques, like atomic force microscopy and traction force microscopy (AFM, TFM). For other diseases like brain disorders, mechanical effects on cells and their impact on disease progression are less studied. Our collaborators of the Vall d'Hebron Institute of Research (VHIR) developed genetically modified cell lines and rodent models of Parkinson's disease (PD) to study the accumulation of neuromelanin (NM) in these systems[a,b]. NM is a dark pigment associated with PD progression. In this work, we studied TR5TY6 neurons from human neuroblastoma overexpressing tyrosinase, a NM-producing enzyme, by mechanical measurements with the AFM. Using our novel model for quantitative data analysis[c], we observed important morphological transformations in the neuronal topography upon NM accumulation, accompanied by up to 2 orders of magnitude increase in cell stiffness. These findings point toward a relevant mechanical dimension at the cellular level in this neurological disease, whose detection by AFM can contribute to a better understanding of the PD disease mechanism.

[a] I. Carballo-Carbajal et al. *Nat Commun* 2019, https://doi.org/10.1038/s41467-019-08858-y.

[b] A. Laguna et al. *Nat Commun* 2024, https://doi.org/10.1038/s41467-024-53168-7.

[c] G.Gomila et al. *ArXiv*, https://doi.org/10.48550/arXiv.2607.22167.

POSTER 98 presented by:
NAME: Beatriz Cantero Nieto

Chemically Fueled Lipid Vesicles as Transient Biomimetic Compartments: Insights from Solution-State AFM

Beatriz Cantero Nieto [1,2], Annalisa Calò[1,2], Gabriel Gomila[1,2], Mohit Kumar[1,3,4]

[1] Institute for Bioengineering of Catalonia, c/ Baldiri i Reixac 11-15, 08028, Barcelona, Spain.
[2] Department of Electronic, Biomedical and Telecommunication Engineering, Physics Faculty of the University of Barcelona, C/ Martí i Franquès 1, 08028, Barcelona, Spain
[3] Department of Inorganic and Organic Chemistry, University of Barcelona, Calle Marti i Fraquès 1-11, 08028 Barcelona, Spain.
[4] Institut de Química Teòrica i Computacional, University of Barcelona, 08028 Barcelona, Spain.

Living membranes are continuously remodeled through chemically driven synthesis and degradation, a behavior that remains difficult to reproduce synthetically. Here we present two classes of synthetic, chemically fueled lipid vesicles, i.e lipase-responsive and pH-responsive vesicles, whose assembly and disassembly can be triggered and temporally programmed through distinct chemical pathways. By mimicking the fuel-driven remodeling of native cell membranes, these transient compartments offer a promising platform for adaptive, stimuli-responsive applications such as controlled drug delivery [1].

Very few techniques are available for the functional imaging of these vesicles at the nanoscale under dynamic processes. To capture the structural evolution of both vesicle types directly in their native, hydrated state, we present atomic force microscopy (AFM) measurements performed in solution, providing nanoscale, time-resolved characterization of their dynamic assembly and disassembly. Vesicles were immobilized on a biotin–streptavidin-functionalized supported lipid bilayer, which stabilizes them, allowing for repeated imaging during disassembly. AFM findings also showed that the surface behavior of both vesicles is markedly different from bulk disassembly. For this reason, typical chemical reactions were also induced directly on non-functionalized substrates (bare mica), to get an overall understanding of surface mediated adsorption and further validate the observed behavior. Our findings show that the AFM technique can allow investigating synthetic membranes which are a step closer to the dynamic, life-like behavior of their biological counterparts, offering a nanoscale framework for their dynamic imaging beyond bulk characterization techniques and optical microscopy at lower resolution.

[1] A. Venugopal, S. Ghosh, A. Calò, G. M. Tuveri, G. Battaglia, M. Kumar, *Angew. Chem. Int. Ed.* 2025, 64, e202500824. https://doi.org/10.1002/anie.202500824

POSTER | MECHANOBIOLOGY

POSTER 99 presented by:

NAME: Carolina Rodríguez Gallo

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

Carolina Rodríguez-Gallo, Timothée Caboche, Chiara Ninfali, Juanma Fernandez Costa, Javier Ramon Azcon

IBEC, Barcelona, Barcelona, Spain

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, environmental stiffness is fixed, and the tissues can only be electrically stimulated. To overcome these limitations, we created 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 nanoparticles within the flexible pillars supporting the tissue. By aligning the magnetic moment of these particles, we can induce a magnetic torque to bend the pillar 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 in the μN range. This innovation opens avenues for numerous research projects, including systematically investigating the tension-differentiation relationship and inducing fiber damage. Additionally, it facilitates the discovery of new disease phenotypes and outcomes, which can be leveraged for subsequent drug screening assays.

[1] Nature Reviews Bioengineering 1, 545–559 (2023)

[2] Biofabrication 15 045024 (2023).

[3] Microsystems & Nanoengineering 9, 153 (2023)

POSTER 100 presented by:
NAME: Elena Faustini

Rational development of a mechanosensitive transcription factor to control gene expression at will

Elena Faustini[1], Miguel González Martinez[1] and Pere Roca-Cusachs[1,2]

[1] Institute for Bioengineering of Catalonia (IBEC), Spain
[2] University of Barcelona (UB), Spain

Cells respond to mechanical forces by converting them into biochemical signals, a process known as mechanotransduction. Forces applied to the nucleus can deform chromatin and nucleoskeletal proteins and alter nuclear pore complex (NPC) conformation. NPC dilation increases molecular transport, with a greater effect on facilitated than passive diffusion, leading to the nuclear import of transcription factors such as YAP, Twist, SMAD, and MyoD. The molecular weight of the molecule and the affinity of its localization sequences for nuclear transport receptors could be exploited to engineer mechanically regulated molecules.

To test the possibility of externally modulating the localization of a molecule, we engineered the tetracycline-controlled transcription factor tTA with different localization peptide sequences, such as nuclear localization (NLS), nuclear export (NES) signals, or cytoplasmic retention sequences (CRS). To determine whether any of these sequences could confer mechanosensitivity to tTA, cells were plated on soft and stiff gels and nuclear to cytoplasmic ratios were quantified.

We first showed that the addition of localization peptides can modulate tTA localization. Some variants also exhibited mechanosensitive import or export behaviour. Moreover, preliminary data showed that engineered tTA can drive the expression of a functional gene in addition to a reporter gene. Together, these results support the development of synthetic transcription factors for mechanically controlled gene expression.

POSTER | MECHANOBIOLOGY

POSTER 101 presented by:

NAME: Elia López Serrano

DNA-based phantom cells for local mechanochemical control of intestinal organoids homeostasis

Elia López Serrano[1,4], Tobias Walter[2], Manuel Gómez-González[1,5], Pere Roca- Cusachs[1,6], Kerstin Göpfrich[2], Xavier Trepat[1,3,4]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2] Center for Molecular Biology of Heidelberg University (ZMBH), Biophysical Engineering Group, Heidelberg University, Heidelberg, Germany, Cluster of Excellence SynthImmune, Heidelberg University, Heidelberg, Germany
[3] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain
[4] Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Barcelona, Spain
[5] Departament de Genètica, Microbiologia I Estadística, Facultat de Biologia, Universitat de Barcelona, Barcelona, Spain
[6] Facultat de Medicina, Universitat de Barcelona, Barcelona, Spain

The intestinal epithelium undergoes constant self-renewal, coordinated in space and time by chemical and mechanical cues to maintain homeostasis. Current organoid models capture bulk biophysical and biochemical control but fail to reproduce the local, cell-scale signaling that governs tissue self-organization in vivo, highlighting the need for a platform with finer spatiotemporal resolution. A discrete, cell-sized unit with defined mechanical properties, embedded within an organoid monolayer, can offer that resolution. Among candidate materials, DNA stands out for its structural versatility and programmability. Building on this, we aim to develop multifunctional, cell-sized DNA hydrogel microparticles (DNA-HPMs) as “phantom cells” by equipping them with sensing and actuation capabilities, designed to locally read out and perturb their microenvironment. The DNA-HMPs self-assemble from DNA nanostars and a complementary linker that binds them together, forming a hydrogel DNA network within water-in-oil droplets. This process yields stable, size-sortable, micrometer-scale hydrogel particles compatible with cell culture conditions. Their stiffness is sequenceprogrammable. Other physico-chemical properties can be tuned during or after formation, through different types of modifications. For example, incorporating paramagnetic particles enables magnetic manipulation and could enhance substrate adhesion. In addition, surface chemistry functionalization allows coating the beads with lipid vesicles for a more cell-like surface, as well as with antibodies against E-cadherin, a key adhesion protein in cell-cell interactions. Preliminary experiments with MDCK epithelial monolayers point to possible interaction between these functionalized DNA beads and surrounding cells. Together, these results represent a first step toward a phantom-cell-based organoid technology that could ultimately help dissect the mechanisms of intestinal homeostasis and how they break down during aging or cancertherapy-induced tissue damage.

POSTER 102 presented by:
NAME: Francesca Mauro

Photo-Responsive Hydrogels With Tunable Stiffness For Cell Mechanobiology

Francesca Mauro[1], Manuel Salmeron-Sanchez[1,2,3]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Spain
[2] Centre for the Cellular Microenvironment, University of Glasgow, UK
[3] Institució Catalana de Recerca i Estudis Avançats (ICREA), Spain

Chronic liver diseases lead to approximately 2 million deaths each year. Fibrosis—driven by the excessive deposition of extracellular matrix produced by activated hepatic stellate cells—is the primary risk factor for hepatocellular carcinoma. Despite its clinical relevance, effective antifibrotic treatments remain limited and often burdened by significant side effects. Immune-based cell therapies, especially those involving macrophages, offer a promising avenue for liver regeneration; however, their therapeutic impact has so far been limited, likely because current strategies fail to induce a durable, antifibrotic macrophage state.

This work aims to overcome this limitation by developing a new therapeutic approach that “primes” macrophages through mechanical stimulation. The strategy exploits mechanical memory, a long-lasting cellular program that persists even after mechanical cues are removed.

To achieve this, we engineered a light-responsive hydrogel composed of chitosan, a highly biocompatible natural polymer, cross-linked with azobenzene functionalized genipin to enable on-demand modulation of stiffness. This platform aims to deliver precisely controlled spatiotemporal mechanical cues to macrophages, steering them toward an anti-inflammatory phenotype and ultimately offering a promising route to restore liver functionality.

POSTER | MECHANOBIOLOGY

POSTER 103 presented by:

NAME: Gotthold Flaeschner

Nuclear geometry predicts local nuclear pore dilation through envelope strain

Gotthold Fläschner[1,], Marc Molina-Jordán[1,*], Anabel-Lise Lle Roux[1], Timon André[2], Aina Albajar[1,3], Roi Eliasan[4], Cristina de la Parte[5], Maddi Garcia-Ayerbe[5], Miguel González- Martín[1], Ignasi Granero-Moya[1], Wanlu Zhang[2], Joaquim Torra[6], Xavier Trepat[1,7], Jan Ellenberg[2,8], María García-Parajó[6,7], Barak Raveh[4], Jonas Ries[2,10*] Ion Andreu[5,10*], Pere Roca-Cusachs[1,3*].*

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), 08028 Barcelona, Spain;
[2] Cell Biology and Biophysics Unit, European Molecular Biology Laboratory, 69117 Heidelberg, Germany;
[3] University of Barcelona, 08028 Barcelona, Spain;
[4] School of Computer Science and Engineering, The Hebrew University of Jerusalem, Jerusalem, Israel;
[5] Instituto Biofisika (UPV/EHU, CSIC), University of the Basque Country, E-48940, Leioa, Spain;
[6] ICFO-Institut de Ciències Fotòniques, The Barcelona Institute of Science and Technology, 08860 Barcelona, Spain
[7] Institució Catalana de Recerca i Estudis Avançats (ICREA), 08010 Barcelona, Spain;
[8] Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Science for Life Laboratory, Tomtebodavägen 23A, SE-171 65 Solna, Sweden;
[9] Max Perutz Labs, University of Vienna, Vienna, Austria;
[10] Ikerbasque, Basque Foundation for Science, 48013, Bilbao, Spain.

Biological shapes encode information about the mechanical forces that generate them and could thereby reveal the state of mechanosensitive molecular structures. Here, we establish such a shape–mechanics–molecule relationship for the eukaryotic cell nucleus, a mechanically loaded organelle whose envelope regulates molecular exchange through nuclear pore complexes (NPCs). We show that micrometre-scale nuclear geometry predicts, across the nuclear envelope, the spatial pattern of both mechanical tension and the nanometrescale dilation state of individual NPCs. Combining imaging with theoretical and computational modelling, we demonstrate that nuclear shape and the resulting spatial distribution of envelope tension emerge from the interplay between isotropic nuclear pressure and anisotropic external forces. Super-resolution imaging further reveals that tension dilates both the NPC inner ring and its central transport channel, increasing nucleocytoplasmic transport. This relationship enables nuclear shape to report through a unified framework how perturbations including osmotic pressure, cytoskeletal contractility and substrate stiffness redistribute envelope tension and alter NPC conformation. Our results establish biological shape as a quantitative bridge between cellular-scale mechanics and molecular-scale mechanosensitive conformational states.

POSTER 104 presented by:
NAME: Guillermo Martínez Ara

An optogenetic toolset to understand and control epithelial mechanical balance

Guillermo Martínez Ara, Emmanuel Spanoudakis & Xavier Trepat Guixer

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.

1 Heisenberg, Carl-Philipp, and Yohanns Bellaïche. "Forces in tissue morphogenesis and patterning." Cell 153.5 (2013): 948-962.

2 Matejčić, Marija, and Xavier Trepat. "Mechanobiological approaches to synthetic morphogenesis: learning by building." Trends in Cell Biology 33.2 (2023): 95-111.

3 Valon, Léo, et al. "Optogenetic control of cellular forces and mechanotransduction." Nature communications 8.1 (2017): 14396.

4 Izquierdo, Emiliano, Theresa Quinkler, and Stefano De Renzis. "Guided morphogenesis through optogenetic activation of Rho signalling during early Drosophila embryogenesis." Nature communications 9.1 (2018): 2366

5 Martínez-Ara, Guillermo, et al. "Optogenetic control of apical constriction induces synthetic morphogenesis in mammalian tissues." Nature Communications 13.1 (2022): 5400.

6 Alt, Silvanus, Poulami Ganguly, and Guillaume Salbreux. "Vertex models: from cell mechanics to tissue morphogenesis." Philosophical Transactions of the Royal Society B: Biological Sciences 372.1720 (2017): 20150520.

POSTER | MECHANOBIOLOGY

POSTER 105 presented by:

NAME: Jorge Oliver-De La Cruz

Mechanical cues regulate Tau axonal localization through microtubule stabilization

Oliver-De La Cruz J[1,2], González-Martín M[1], Altadill Cordero M[1], Del Río JA[1,2], Paganetti P[3,4], Roca-Cusachs P[1,5]

[1] *Institute for Bioengineering of Catalonia, Barcelona, Spain*
[2] *Facultat de Biologia, Universitat de Barcelona, Barcelona, Spain*
[3] *Faculty of Biomedical Sciences, Università della Svizzera Italiana, Lugano, Switzerland*
[4] *Laboratory for Aging Disorders, LRT, Ente Ospedaliero Cantonale, Bellinzona, Switzerland*
[5] *Facultat de Medicina, Universitat de Barcelona, Barcelona, Spain*

Brain tissue undergoes substantial changes in its mechanical properties during development, aging, and neurodegenerative disease. In Alzheimer's disease (AD), these alterations occur alongside cytoskeletal dysfunction and Tau pathology, yet their contribution to neuronal dysfunction remains poorly understood.

To investigate how extracellular mechanics regulate neuronal homeostasis, we cultured NGN2-differentiated SH-SY5Y-derived neurons on laminin-functionalized polyacrylamide hydrogels of different stiffnesses. Softer substrates reduced neuronal spreading and neurite extension. Pharmacological perturbations showed that Rho-associated contractility contributes to this response, while microtubule stability becomes critical for neurite maintenance once processes are established. Consistently, compliant substrates reduced the polarization of stable, acetylated microtubules.

These cytoskeletal changes were accompanied by increased Tau phosphorylation and redistribution from neurites towards perinuclear and nuclear compartments. In MAPT-knockout neurons reconstituted with fluorescent Tau, compliant substrates also increased axonal Tau mobility, consistent with reduced microtubule association. Furthermore, substrate stiffness modulated the susceptibility of Tau to seeded accumulation.

These effects were reproduced in primary embryonic hippocampal neurons and confirmed in human iPSC-derived neurons. Notably, reducing stiffness in isogenic APOE3/E3 neurons induced alterations in Tau phosphorylation and localization that partially resembled the basal APOE4/E4 phenotype.

Together, our results identify extracellular stiffness as a regulator of neuronal cytoskeletal organization and Tau homeostasis, linking mechanical cues to Tau localization, dynamics, and pathological recruitment in AD.

POSTER 106 presented by:

NAME: Margherita Gallano

Nuclear Envelope Remodelling upon Mechanical Perturbation

Margherita Gallano [1,2], Aina Albajar Sigalés [1,2], Evelyn Coderch Bifet [1], Miguel González Martín [1], Valeria Venturini [1], Nimesh Chahare [3], Anabel-Lise Le Roux [1], Pere Roca- Cusachs [1,2]

[1] Institute for Bioengineering of Catalonia (IBEC)
[2] University of Barcelona (UB)
[3] EMBL Barcelona

Cells experience mechanical loads during many fundamental processes, including growth, differentiation, and migration. These forces are transmitted to the nucleus and can influence gene expression, ultimately modulating cell behaviour and determining cell fate. The Nuclear Envelope (NE) plays a critical role in this process, as it has been shown to sense cell size variations and activate mechanosensitive signalling pathways. Yet, the phenomenology of NE responses to mechanical stimuli remains largely unexplored. In this project, we aim to characterize the dynamic response of the NE under both stretch and compression. We employ a custom-made microfluidics device to apply controlled stretch to isolated nuclei (iNuclei) from HeLa cells anchored onto a stretchable PDMS membrane. Our results demonstrate that isolated nuclei undergo NE remodelling upon strain application, characterised by flattening of nuclear envelope wrinkles and increase in nuclear volume. Interestingly, we observe an auxetic deformation of the iNuclei: as the stretch is being applied to the PDMS membrane, the nuclear height increases. We use a nanoindenter combined with a confocal microscope with high temporal resolution to observe the NE response to compressive loads on single HeLa cells and iNuclei. Using single cells and isolated nuclei as model systems, we aim to distinguish active from passive processes of NE remodelling. In indentation experiments on intact cells, we observe rapid NE wrinkling upon release of the compression, followed by a gradual restoration of the original nuclear morphology. We will next investigate how each NE component contributes to the recovery dynamics after compression by selectively perturbing the system and observing the resulting response.

POSTER | MECHANOBIOLOGY

POSTER 107 presented by:

NAME: Marina Placci

Redefining Membrane Nanomechanics in Lysosomal Disorders: The Role of GlcCer and Gb3

Marina Placci[1,2,3], Stefano Chiodini[1,4], Mireia Casampere Ferrer[5], Silvia Muro[2,6], Marina I. Giannotti[1,4,7]

[1] *Nanoprobes & Nanoswitches Group, IBEC, BIST. Spain.*
[2] *Targeted Therapeutics and Nanodevices Group, IBEC, BIST. Spain.*
[3] *Doctoral Program in Biotechnology, Faculty of Pharmacy and Food Sciences, University of Barcelona (UB). Spain.*
[4] *CIBER-BBN, ISCIII. Spain.*
[5] *Department of Biological Chemistry, Research Unit on BioActive Molecules, IQACCSIC. Spain.*
[6] *ICREA. Spain.*
[7] *Department of Materials Science and Physical Chemistry, IQTC, UB. Spain.*

Lysosomal storage disorders (LSDs) are a group of rare inherited metabolic diseases characterized by deficiencies in lysosomal components that lead to the pathological accumulation of undegraded substrates inside cells. In Gaucher (GD) and Fabry (FD) diseases, enzyme defects drive the cellular buildup of specific glycosphingolipids (GSLs)—glucosylceramide (GlcCer) and globotriaosylceramide (Gb3), respectively— leading to compromised endocytic trafficking and altered cellular biology. However, how this physical lipid accumulation alters membrane organization and cell mechanics remains poorly understood.

In this work, we used Atomic Force Microscopy (AFM) and force spectroscopy to study these mechanical alterations across synthetic model membranes (supported lipid bilayers, SLBs) and patient-derived cells. In model membranes, GlcCer and Gb3 showed distinct physical behaviors: GlcCer increased lipid packing and mechanical resistance, while Gb3 caused domain expansion up to a phase inversion in the bilayer. In patient-derived fibroblasts, lipidomic analysis confirmed that GSL accumulation altered plasma membrane composition, especially after metabolic stimulation with sphingosine. In cell mechanics experiments, tether pulling force measurements showed higher pulling forces in GD cells, pointing to increased membrane stiffness and higher in-plane tension. FD cells also showed elevated tether forces, which notably decreased following metabolic stimulation. Measuring overall cell stiffness through indentation showed that FD cells were mostly unchanged near the surface but became stiffer at deeper indentation levels after metabolic stimulation.

Finally, preliminary recombinant human α-galactosidase A treatment cleared accumulated Gb3 and showed initial mechanical recovery in FD cell models. Overall, this study shows how specific lipid species physically alter cell membranes, helping us better understand how molecular accumulation leads to mechanical dysfunction in LSDs.

POSTER 108 presented by:

NAME: Miguel González Martín

Design of synthetic mechanosensitive transcription factors

Miguel González-Martín[1], Elena Faustini[1], Juan M. Portilla[2], Marta Badia[1], Marc Molina[1], Ignasi Granero-Moya[1], Dimitrije Ivančić[3], Benedetta Bolognesi[1], Ion Andreu[4], Marc Güell[2] and Pere Roca-Cusachs[1].

[1] Institute for Bioengineering of Catalonia (IBEC),Barcelona, Spain
[2] Department of Medicine and Life Sciences, University Pompeu Fabra, Barcelona, Spain
[3] Wyss Institute for Biologically Inspired Engineering at Harvard University, Boston, USA
[4] Instituto Biofisika (IBF), Leioa, Spain

Cells sense mechanical signals through a process known as mechanotransduction, activating signaling pathways that regulate cell behavior in health and disease. Exogenously controlling mechanotransduction would be very useful for both fundamental research and potential diagnostic or therapeutic applications, yet it remains a challenge to do so in a predictable and programmable manner. Here, we developed a quantitative screening platform for engineering synthetic mechanosensitive transcription factors (mSynTFs) that directly couple force-dependent changes in nucleocytoplasmic transport to gene regulation. This platform exploits the mechanical regulation of passive and facilitated nuclear transport to tune the force-responsive localization of mSynTFs. Such mSynTFs aim to recapitulate the localization behavior of endogenous mechanosensitive proteins such as YAP and Twist, while driving the expression of selected target genes in a controlled way. To achieve this, we established a novel reporter-cell screening platform incorporating substrates of different stiffnesses. This platform enables high-throughput screening of mSynTF libraries, facilitating the identification of variants with higher mechanosensitivity, while providing quantitative insight into the molecular features that make a transcription factor mechanosensitive. Beyond generating a new class of synthetic transcription factors, this work establishes a framework for dissecting the minimal design principles underlying mechanoregulation of gene expression. We envision that programmable mSynTFs will provide a versatile interface between the cellular mechanical environment and synthetic gene circuits, enabling mechanically controlled transcriptional programs and expanding the toolkit for engineering complex cellular behaviors in synthetic biology.

POSTER | MECHANOBIOLOGY

POSTER 109 presented by:

NAME: Mireia Valero Puigdomenech

Effects of matrix viscoelasticity on macrophages polarization and their interactions with mesenchymal stem cells

Mireia Valero Puigdomenech[1], Mariana Azevedo González Oliva[1], Manuel Salmeron- Sanchez[1,2]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Spain.
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA), Spain.

Macrophages are innate immune cells involved in homeostasis, development, tissue repair and immunity[1]. Their phenotype can shift along a continuum from pro-inflammatory (M1-like) to pro-regenerative (M2-like) states in response to biochemical and biophysical microenvironmental signals. Macrophage phenotype can also influence mesenchymal stem cell (MSC) behaviour[2]. Although the impact of extracellular matrix (ECM) elasticity on macrophages has been studied and shown to regulate their behavior[3], little is known about the effects of matrix viscoelasticity on macrophage polarization and macrophageMSC interactions[4]. Our aim is to investigate how local mechanics, especially viscoelasticity, influence macrophage polarization and their interactions with MSCs in 3D hydrogel systems.

Polyethylene glycol-based hydrogels functionalized with full-length fibronectin (PEG-FN) are being developed to support cell-matrix interactions[5]. By modifying crosslinking density and polymer molecular weights, we generate families of soft and stiff hydrogels with elastic or viscoelastic properties. Their mechanical properties are quantified by nanoindentation and rheology. Human macrophages and MSC spheroids are encapsulated within these matrices, and their morphology and organization are assessed using confocal microscopy. Brillouin spectroscopy allows contact-free, real-time characterization of the samples to obtain spectral data related to mechanical properties of cells and hydrogels over time. The next steps will focus on further developing the PEG-based hydrogel platform and carrying out the first experiments with primary macrophages.

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 better physiologically relevant biomaterials.

We acknowledge financial support from the ERC Advanced Grant Devise 101054728 to M.S.S.

References: [1] Wynn et al, *Nature*, 2013; [2] Fan et al, *Front. Cell Dev. Biol.*, 2023; [3] D'Ambrosio et al, *Front. Immunol.*, 2026; [4] Tao et al, *Adv. Healthc. Mater.*, 2025; [5] Trujillo et al, *Biomaterials*, 2020.

POSTER 110 presented by:
NAME: Ona Baguer Colomer

Nuclear mechanics integrate chemical and physical cues to regulate EMT in pancreatic cancer cells

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

[1] *Institute for Bioengineering of Catalonia (IBEC), Spain*
[2] *University of Barcelona (UB), Spain*
[3] *Spanish National Cancer Research Centre (CNIO), Spain*
[4] *Pompeu Fabra University (UPF), Spain*

The epithelial-to-mesenchymal transition (EMT) is an important event that regulates the progression of solid tumours. EMT is known to be triggered by both chemical and physical cues, but how cells integrate these factors is not well understood. To address this question, we induced EMT in a pancreatic cancer cell model chemically with TGF-β and physically by controlling substrate stiffness and cell spatial positioning. Specifically, we patterned circular monolayers onto hydrogels of different rigidities and treated them with or without TGF-β. We found that EMT was more strongly induced in colony regions with lower local cell density. TGF-β1 was required for this response, whereas the main contribution of substrate stiffness was to promote greater cell spreading and migration, thereby facilitating the formation of lower-density regions. This low-density EMT pattern was predominantly associated with nuclear deformation, and perturbation of nuclear mechanical properties altered the EMT phenotype of the cells. Altogether, these results demonstrate that nuclear mechanics fine-tunes the mechanochemical integration that drives different EMT phenotypes, with relevance to pathologies exhibiting mechanical alterations, such as pancreatic cancer.

Keywords: nuclear mechanics, EMT, nuclear lamina, pancreatic cancer.

POSTER | MECHANOBIOLOGY

POSTER 111 presented by:

NAME: Pierre Ucla

From 2D to 3D: CAF Mechanotransduction in Fibrillar Microenvironments

Pierre Ucla[1], Manuel Salmeron-Sanchez[1,2,3], Pere Roca-Cusachs[1,4]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain
[2] Centre for the Cellular Microenvironment (CeMi), The Advanced Research Centre, University of Glasgow, Glasgow, UK
[3] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain
[4] University of Barcelona, Barcelona, Spain

Mechanotransduction is a key regulator of cancer-associated fibroblast (CAF) behavior, particularly in pancreatic ductal adenocarcinoma (PDAC), where CAFs generate and remodel a dense, fibrotic, and highly anisotropic extracellular matrix. Although mechanotransduction frameworks such as the molecular clutch have established how cells sense and transmit forces in 2D, how these principles operate within fibrous 3D matrices remains poorly understood. In particular, it remains unclear how the spatial organization and mechanical properties of individual fibers are integrated by the cell to regulate cytoskeletal force transmission, nuclear mechanics, and fibroblast activation.

Here, we use a synthetic 3D fibrillar platform that independently controls fiber organization, stiffness, density, and 3D extension, enabling a continuous transition from 2D-like to multilayered 3D environments. We investigate how these physical architectures reshape the cellular force machinery and propagate mechanical information from the extracellular matrix to the nucleus, combining analysis of actin and focal adhesions with quantitative characterization of nuclear 3D morphology, nuclear-envelope folding, and YAP localization, complemented by Brillouin microscopy. We further determine how these mechanical states influence CAF activation and contractility.

By systematically linking extracellular architecture to cellular force transmission, nuclear mechanotransduction, and fibroblast activation, this project aims to establish a general framework for understanding mechanobiology in fibrous 3D environments, while revealing how stromal architecture may contribute to CAF-driven remodeling and tumor progression in PDAC.

POSTER 112 presented by:

NAME: Ricard Casanovas Zapata

Mechanobiology of Differentiating hiPSC Colonies

Ricard Casanovas Zapata[1], Özge Özgüc[1], Miquel Bosch Padrós[1], Aina Ventura Porcar[1], Steffen Grosser[1], Tim Dullweber[2], David Brückner[2], Xavier Trepat[1,3]

[1] IBEC, Barcelona, Spain
[2] UNIBAS, Basel, Switzerland
[3] ICREA, Barcelona, Spain

Over the last decade, the emergence of hPSC-based models has provided significant insight into early human developmental events that are otherwise difficult to study due to both ethical constraints and physical inaccessibility. While phenomena such as gene patterning and axis specification have been widely investigated, the mechanical processes underlying these events remain comparatively understudied, despite evidence of their key role. We use micropatterned hPSC colonies, including the 2D gastruloid model whose biochemical evolution is well characterized, to investigate the mechanobiology of the same cell types that make up the post-implantation human embryo.

To interrogate how cells jointly integrate mechanics and signalling during differentiation, we combine 2.5D traction force microscopy to extract spatiotemporal force patterns with immunostaining-based readouts of signalling and lineage markers, while live imaging and single-cell tracking capture the evolving collective dynamics of the colonies. This multimodal approach enables us to follow not only the lineages cells adopt, but also how they mechanically and dynamically change their fate in real time.

The co-evolution of biomechanics and biochemistry in such a controllable system opens the door to addressing classically inaccessible questions in human development, including how initially homogeneous cell populations undergo symmetry breaking and generate organized multicellular behaviours. For example, we are now able to track the mechanical signature of differentiating colonies as they establish the three germ layer -like structure. Ultimately, our system provides a tractable platform with which to explore fundamental principles guiding early human embryogenesis.

POSTER MECHANOBIOLOGY

POSTER 113 presented by:

NAME: Rohit Nautiyal

Nematically guided fracture in brain endothelia

Rohit Nautiyal[1 2], Pau Guillamat[1], Xavier Trepat[1 2 3 4]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain.
[2] Department of Biomedicine of the Faculty of Medicine and Health Sciences, University of Barcelona, Barcelona, Spain.
[3] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.
[4] Biomedical Research Networking Center in Bioengineering, Biomaterials, Nanomedicine (CIBER-BBN) Barcelona, Spain

Brain endothelial cells (BECs) lining the blood vessels and capillaries continuously experience mechanical stress, such as shear stress and stretch, as a part of their normal physiological function. These cells continuously adapt to these stresses by actively reorganizing their orientation, cytoskeletal architecture, and cell-cell junctions maintaining barrier integrity[1]. Under disturbed flows or pathological conditions like chronic inflammation, parasitic infection or cancer, this adaptation fails, leading to gap formation between endothelial cells, increasing paracellular permeability and leading to barrier dysfunction[2]. Although the molecular mechanisms of gap formation including tight junction and cytoskeletal remodelling, are well characterized[3,4], the mechanical principles governing endothelial fractures remain unresolved. In particular, how orientational (nematic) order and local regions of disorder, such as topological defects, mechanically regulate gap nucleation and subsequent fracture dynamics in endothelia remains unknown.

Here, we investigate the fracture dynamics in nematically ordered BEC monolayers subjected to enzymatic perturbations. We find that fracture preferentially nucleates close to regions of low orientational order, including topological defects. Force maps obtained by Traction force microscopy revealed concentration of forces around topological defect sites relative to aligned regions in the monolayer, suggesting that active stresses at these low order regions might be a cause for facilitated fracture initiation. Taken together, our results identify orientational order as a key mechanical regulator of endothelial gap formation and provide a physical framework linking collective cell organization to barrier disruption in brain endothelia.

References

1. Dessalles, Claire A., et al. "Integration of substrate-and flow-derived stresses in endothelial cell mechanobiology." *Communications Biology* 4.1 (2021): 764.

2. Carman, Christopher V., et al. "Transcellular diapedesis is initiated by invasive podosomes." Immunity 26.6 (2007): 784-797.

3. Gopal, Sowmya Shree, et al. "The breakdown of neurovascular barriers: molecular mechanisms of tight junction dysfunction." *Molecular Neurobiology* 63.1 (2026): 273.

4. Abikenari, Matthew, et al. "Molecular and biophysical remodeling of the blood–brain barrier in glioblastoma: mechanistic drivers of tumor–neurovascular crosstalk." *Frontiers in Physics* 13 (2025): 1723329.

POSTER 114 presented by:

NAME: Steffen Grosser

Cell contractility controls epithelial tissues across timescales

Steffen Grosser[1], Alba López Rivas[1,2], Ricard Alert[2, 3, 4, 5, 6, 7], Xavier Trepat[1,2,7,8]

[1] *IBEC, Barcelona, Spain*
[2] *UB, Barcelona, Spain*
[3] *UB Institute of Complex Systems (UBICS), Barcelona, Spain*
[4] *Max Planck Institute for the Physics of Complex Systems, Dresden, Germany*
[5] *Center for Systems Biology Dresden, Dresden, Germany*
[6] *Cluster of Excellence Physics of Life, TU Dresden, Dresden, Germany*
[7] *Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain*
[8] *Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina, Barcelona, Spain*

A central mechanical function of cells is to exert contractile forces that are important during, e.g., cell motility and division. However, how and if such contractile forces coordinate and control epithelial tissue architecture and state on the mesoscale is still elusive. Here, we use optogenetics to exert precise spatial and temporal control over the contractility of cells in an epithelial tissue. By shining light on a region of a tissue, we can increase RhoA activity in it on demand, tuning the cell contractility. We measure the mechanical impact via traction force microscopy (TFM) and the architecture (cell shapes and sizes) via segmentation. We find that first, activating RhoA immediately leads to an increased contractile tension in the cells. Second, surprisingly, cell shapes in activated regions elongate on the timescale of minutes to hours, which increases cell motility. Against assumptions held in the field, increased contractile forces could contribute to fluidizing and mobilizing cells in tissues. On longer timescales of hours to tens of hours, the tension over activated areas makes the tissue slowly contract. Measuring stress and strain, we construct an effective long-timescale optogenetic tissue rheometer. Lastly, by activating contractility over even longer timescales of days, we create regions of increased densities - up to the millimeter scale. This asks to what extent the homeostatic tissue state and density are actively controlled by contractility.

POSTER | MECHANOBIOLOGY

POSTER 115 presented by:

NAME: Vladislav Petrovskii

Diffusion Anisotropy in Ionically Linked Copolymers

Vladislav S. Petrovskii and Cesar Rodriguez-Emmenegger

We recently demonstrated that ionically linked comb polymers [1,2], consisting of cationic polymer backbones dynamically connected to anionic ligands through reversible ionic interactions, can self-assemble into giant unilamellar vesicles. These membranes reproduce several fundamental properties of their biological counterparts, including membrane thickness, bending rigidity, and lateral diffusion, making them a promising platform for the construction of artificial cells. At the same time, their unusual molecular architecture, in which the hydrophilic polymer backbones are spatially separated from the hydrophobic ligand core, gives rise to physical phenomena that are not typically observed in conventional liposomes or polymersomes.

Two particularly interesting effects are the nematic ordering of the polymer backbones induced by their two-dimensional confinement within the membrane and the resulting anisotropic lateral diffusion of both the backbones and the ionically associated ligands. Here, we investigate these phenomena using molecular dynamics simulations at two levels of resolution: fully atomistic simulations and coarse-grained simulations based on the MARTINI force field. We systematically explore the molecular parameters controlling diffusion anisotropy in both membrane components. For the ligands, we vary the length of the hydrophobic tails, while for the polymer backbones, we vary the degree of polymerization to quantify its effect on orientational ordering and anisotropic transport. Our results reveal how the molecular architecture of ionically linked copolymers couples membrane organization to lateral dynamics and provide design principles for controlling transport in synthetic biomimetic membranes.

References

[1] A. M. Wagner *et al.*, *Advanced Science*, 2022, **9**(17), 2200617.

[2] D. Söder *et al.*, *Advanced Science*, 2025, **12**(15), 2411497.

POSTER 116 presented by:
NAME: Yudish Varma

Mechanosensing through intermediate filaments alone

Yudish Varma[1,2], Elena Faustini[1], Miguel González-Martín[1], Pere Roca-Cusachs[1,2]

[1] Institute for Bioengineering of Catalonia (IBEC), 08028, Barcelona
[2] Faculty of Medicine, Universitat de Barcelona, 08036, Barcelona

Mechanosensing is understood almost entirely through actin-linked focal adhesions. Integrin α6β4 is the exception: via plectin, it couples the matrix directly to keratin intermediate filaments. Our group recently showed that on laminin this linkage stiffens the keratin network and shields the nucleus from actomyosin-driven deformation, impairing rigidity sensing and YAP nuclear localisation — yet blocking β4 altered neither cell forces nor focal adhesions. Whether α6β4 bears load at all cannot be resolved while β1 integrins remain available to compensate.

We are generating β1-depleted MCF10A cells on defined laminin substrates, where α6β4 should become the sole adhesion receptor. After establishing that adhesion is abolished by β4 blockade, we will measure traction, adhesion strength and nuclear deformation across stiffness and laminin isoforms — asking whether intermediate-filament adhesion is a mechanotransducer or a purely passive shield.

FLASH PRESENTATION | MECHANOBIOLOGY

FLASH presented by:

NAME: Mariana Azevedo Gonzalez Oliva

Soft matrix viscoelasticity: from mechanotransduction to neural communication

Mariana A. G. Oliva[1], Manuel Salmeron-Sanchez[1,2,3]

[1] Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Barcelona, Spain
[2] Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain
[3] Centre for the Cellular Microenvironment (CeMi), The Advanced Research Centre, University of Glasgow, Glasgow, UK

The extracellular matrix (ECM) is increasingly recognised to mechanically behave as a viscoelastic solid, exhibiting fluid-like energy loss (viscosity) and solid-like energy storage (elasticity) in response to applied deformations. ECM viscoelasticity has been shown to profoundly influence cell behaviour, including proliferation, differentiation as well as disease progression. Notably, the brain is among the most viscoelastic tissues in the body, and alterations in its mechanical properties are hallmarks of neurodegeneration[1]. However, most in vitro brain models rely on unphysiologically stiff, purely elastic substrates that fail to capture the dynamic mechanics of native tissue[2-3].

Our work has previously demonstrated the importance of the concerted action of Piezo1 and the molecular clutch complex in transducing viscoelasticity[4]. For this, we employed polyacrylamide (PAAm) hydrogels with tuneable elastic and viscous moduli as well as a modified viscoelastic molecular clutch model that incorporated the crosstalk of Piezo1 and integrin complexes. With our experimental set-up we demonstrated integrin–Piezo1 concerted action is a key regulator of the mechanotransduction of viscoelasticity in soft matrices. Building on these findings, we are now extending this approach to neuronal systems to decode how viscoelasticity shapes neuronal mechanosensing, activity, and communication. Using human neuron cell models (SHSYS5-derived and iNeurons), we investigate cell response to physiological and pathological viscoelasticity and assess how and whether these changes influence neuronal communication, investigating the key regulators of circuitry development. By integrating advanced biomaterials, live-cell imaging, and computational modelling, we aim to reveal how the brain microenvironment's dynamic mechanical properties modulate synaptic and cytoskeletal dynamics.

[1] Chaudhuri et al., “Effects of Extracellular Matrix Viscoelasticity on Cellular Behaviour.” [2] Lantoine et al., “Matrix Stiffness Modulates Formation and Activity of Neuronal Networks of Controlled Architectures”; [3]Rabadan et al., “An in Vitro Model of Neuronal Ensembles.” [4]A. G. Oliva et al., “Piezo1 regulates the mechanotransduction of soft matrix viscoelasticity”

FLASH presented by:

NAME: Marija Matejčić

Mechanical Coordination of Intestinal Cell Extrusion by Supracellular 3D Force Patterns

Marija Matejčić[1,], Meng Wang[1], Ronja Houtekamer[2], Elia López Serrano[1], Manuel Gómez-González[1], Miquel Bosch-Padrós[1], Neta Felsenthal[3], Carlos Pérez-González[1,4], Gerardo Ceada[1,5,6,7,8], Pere Roca-Cusachs[1,9], Marino Arroyo[1,10,11], Danijela Matić Vignjević[3], Martijn Gloerich[2], Xavier Trepat[1,12,13,*]*

[1] *Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology (BIST), Barcelona, Spain.*
[2] *Center for Molecular Medicine, University Medical Center Utrecht and Utrecht University, Utrecht, The Netherlands.*
[3] *Institut Curie, PSL Research University, CNRS UMR 144, Paris, France.*
[4] *Inserm U1279, Gustave Roussy Institute, Villejuif, France.*
[5] *Biomedical Research Institute (IDIBELL), L'Hospitalet de Llobregat, Barcelona, Spain.*
[6] *IRTA, Programa de Sanitat Animal, Centre de Recerca en Sanitat Animal (CReSA), Campus de la Universitat Autònoma de Barcelona (UAB), Bellaterra, Barcelona, Spain.*
[7] *Unitat mixta d'Investigació IRTA-UAB en Sanitat Animal, Centre de Recerca en Sanitat Animal (CReSA), Campus de la Universitat Autònoma de Barcelona (UAB), Bellaterra, Barcelona, Spain.*
[8] *Department of Cell Biology, Physiology and Immunology, Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Spain.*
[9] *Facultat de Medicina, Universitat de Barcelona, Barcelona, Spain.*
[10] *LaCàN, Universitat Politècnica de Catalunya–BarcelonaTech, Barcelona, Spain.*
[11] *Centre Internacional de Mètodes Numèrics en Enginyeria (CIMNE), Barcelona, Spain.*
[12] *Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain.*
[13] *Centro de Investigación Biomédica en Red en Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Barcelona, Spain.*

Every day, the mammalian intestinal epithelium extrudes millions of cells to sustain tissue self-renewal. Despite its fundamental role in intestinal homeostasis, the mechanisms that trigger, compartmentalize, and execute intestinal cell extrusion remain poorly understood. Here, using intestinal organoids, we map the three-dimensional forces and cytoskeletal dynamics that drive intestinal cell extrusion. We show that extrusion is initiated by a calcium influx followed by focal adhesion disassembly and the dissolution of a basal actomyosin meshwork. After this initial phase, which occurs under increasing tensile stress, a supracellular three-dimensional pattern of traction forces generates a bending moment that promotes cell expulsion from the monolayer. This three-dimensional force pattern requires myosin contractility and is generated by lamellipodial protrusions in neighboring cells. Importantly, these lamellipodia are required for upward force and torque generation but also determine whether extrusion occurs apically or basally, serving as symmetry breakers in the process. Finally, we show that the compartmentalization of cell extrusion to regions outside the intestinal crypt does not require curvature and instead depends on the activity of myosin 2A along the crypt-villus axis. Together, our findings provide the mechano-chemical mechanism by which intestinal cell extrusion is localized, initiated, and executed under tensile stress of the villus tissue.

FLASH PRESENTATION | SMART DATA ANALYSIS

FLASH 117 presented by:

NAME: Fleur Clemenceau

Simultaneous 12-lead ECG for the validation of novel cellulose-based electrodes in human subjects

Fleur Clemenceau[1], Jaume Rodríguez Soler[1], Ravneet Rahul Sandhu Singh[1], Aleix Martí Maymo[2], Antón Guimerà Brunet[2], Mahtab Mohammadpoor Faskhodi[1], Inés Bueso- Inchausti Garcìa[1], Yolanda Castillo Escario[1], Daniel Romero Pérez[1], Fabiola Vilaseca Morera[3], Gemma Gabriel Buguña[2], Raimon Jané Campos[1]

[1] *Universitat Politècnica de Catalunya (UPC) / Institute of Bioengineering of Catalonia (IBEC) / CIBER-BBN, Barcelona, Spain*
[2] *Institute of Microelectronics of Barcelone (IMB-CNM), Barcelona, Spain*
[3] *Advanced Biomaterials and Nanotechnology, University of Girona, Girona, Spain*

Sustainability is an increasing concern in the medical device field, particularly in electrophysiology. This study evaluates novel cellulose-based ECG electrodes as a more biodegradable alternative to commercial Ag/AgCl electrodes, focusing on their morphology, signal similarity, and their suitability for clinical cardiac diagnosis.

The proposed electrodes consist of three layers: a conductive vegetal cellulose film doped with PEDOT:PSS as the core, an adhesive layer and a hydrogel layer. ECG signals were simultaneously acquired from cellulose-based and standard Ag/AgCl electrodes in ten healthy volunteers (mean age 31 ± 8, 50% male). Recordings were performed in supine resting conditions using the 12-lead configuration and after exercise (2 minutes of jumping jacks) only for leads I, II and V5. ECG signals were pre-processed using high and low-pass Butterworth filters (0.5-40 Hz), and a 50 Hz notch filter to reduce the power-line noise. After signal normalization, we delineated the individual recordings to automatically detect the ECG characteristic points and consequently determine ECG intervals, by using a multilead delineation approach. These intervals included the PR, RR, QRSd, QT, QTc and Tpe. Agreement between electrode types was assessed using Pearson's correlation coefficient and root mean square error (RMSE), while signal quality was evaluated using the basSQI and pSQI metrics.

Results demonstrated a high similarity in both signal morphology and signal quality between cellulose-based and Ag/AgCl electrodes. Pearson correlation coefficients were ≥ 0.965 and RMSE ≤ 0.309, while differences in signal quality metrics remained low, with maximum differences of 0.035 for basSQI and 0.060 for pSQI. ECG intervals differences were within the tolerance values suggested in the literature (10 ms) for PR, RR, QRSd intervals. Larger differences were observed for T-wave-related intervals (QT, QTc and Tpe), mainly due to the difficulty of accurately delineating the end of the T-wave. These results highlight the potential of cellulose-based electrodes as a sustainable alternative to conventional Ag/AgCl electrodes for 12-lead ECG monitoring. Future work will focus on improving T-wave delineation and enabling long-term Holter recordings.

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)

FLASH 118 presented by:
NAME: Lluís Fernández Romero

Curvature Regularized Time Warping for Chromatographic Alignment

L. Fernández[1,2], G. Guedes de la Cruz[2], A. Pardo[2], S. Marco[1,2]

[1] *Department of Electronics and Biomedical Engineering, Universitat de Barcelona, Barcelona, Spain*
[2] *Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain*

Chromatographic time misalignment is a well-known issue in analytical chemistry. It arises from variations in chromatographic conditions and leads to peak shifts along the retention time axis, hindering the direct use of chromatographic data in multivariate analysis. Parametric Time Warping (PTW) provides an efficient solution by explicitly modelling the warping function using low-degree polynomials [1]. However, the use of a predefined functional form may limit its flexibility when more complex time distortions are present.

In this work, we propose Curvature Regularized Time Warping (CRTW), a nonparametric warping approach inspired by PTW. Instead of assuming a specific functional form, CRTW estimates the warping function directly from the data while enforcing smoothness through a penalty on its second derivative. This regularization controls the local curvature of the warping function, preventing abrupt variations in the time transformation while retaining sufficient flexibility to correct nonlinear misalignments.

The method was evaluated using GC-IMS measurements of standard ketone mixtures routinely employed for instrument stability assessment [2]. The results show that CRTW provides accurate alignment across the chromatographic range, reducing peak dispersion and improving reproducibility among repeated measurements.

References

[1] Eilers P.H.C., *Anal. Chem.*, **2004**, 76, 404–411.
[2] G.A.S. Gesellschaft für analytische Sensorsysteme mbH, *GC IMS instrumentation and applications*, Dortmund, Germany.

FLASH PRESENTATION | SMART DATA ANALYSIS

FLASH 119 presented by:

NAME: Mariano Martín

Systematic mutational mapping reveals optimal amyloid formation for RIPK function

Martin M and Bolognesi B

Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology, Barcelona, Spain.

Amyloid formation, typically associated with neurodegeneration, can also serve essential biological functions. RIPK1 and RIPK3 kinases assemble functional amyloids via their RHIM domains to drive necrosome formation and necroptosis. Here, we systematically map the sequence-function relationship of these domains using deep mutagenesis combined with massively parallel assays that directly report on amyloid nucleation and necroptotic signaling. Analysis of ~3,000 mutations across RIPK1 and RIPK3 reveals that both proteins rely on a conserved aliphatic quartet to nucleate amyloids, but diverge mechanistically: RIPK3 nucleation is largely driven by this core interface, whereas RIPK1 requires a second aliphatic surface to achieve efficient nucleation. Cross-species comparisons with mutational atlases from mouse RIPKs show conservation of these principles, underscoring their evolutionary selection. Strikingly, functional outcomes depend on finely balanced nucleation: variants that either reduce or enhance amyloid formation impair necroptosis. Consistently, human population genetics indicates that such variants are extremely rare, suggesting evolutionary optimization of the RHIM domain at a “sweet-spot” of amyloid propensity required for signaling. By linking quantitative mutational landscapes to functional amyloid assembly, this work uncovers how evolution has tuned the amyloid propensity of RIPKs to enable robust cell death signaling. These insights not only advance our understanding of amyloid biology but also provide a framework for therapeutic modulation of necroptosis and for engineering synthetic amyloids with tailored activities.

FLASH 120 presented by:

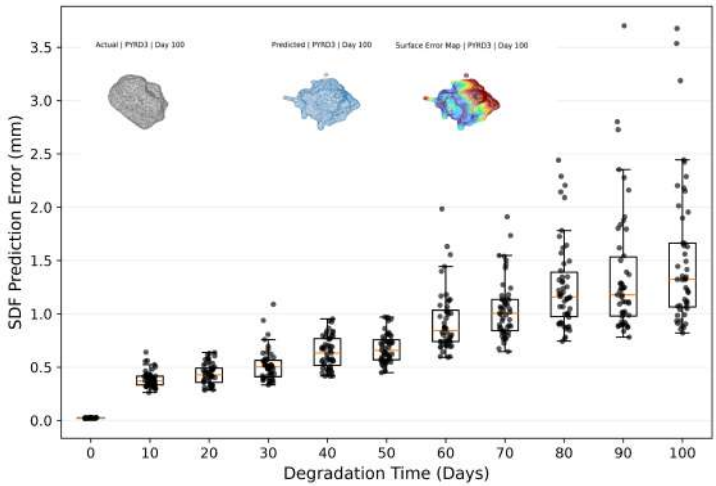
NAME: Revathi Ravindran

Towards a Comprehensive Modelling and Design Framework for Predicting Biodegradation at a Macroscale

Revathi Ravindran[1], Nagarajan Raghavan[1], Stylianos Dritsas[2], Javier Gomez Fernandez[1,3,4]

[1] *Engineering Product Development, Singapore University of Technology and Design, Singapore*
[2] *Architecture and Sustainable Design, Singapore University of Technology and Design, Singapore*
[3] *Institute for Bioengineering of Catalonia*
[4] *ICREA*

Biodegradation remains relatively difficult to predict for three-dimensional structures, as existing approaches predominantly characterize molecular or bulk material changes rather than the geometrical evolution of macroscopic objects. Here, we **present a geometry-driven framework for characterizing and predicting the macroscale biodegradation of three-dimensional objects**. Degradation experiments and high-resolution 3D scanning capture geometric evolution over time, while signed distance fields (SDFs) were used to quantify these geometric changes. With a database of different geometries and degradation time points, a K-nearest neighbours (KNN) based framework was utilized to predict degraded geometries. Experiments revealed **geometry-dependent, spatially non-uniform degradation** and progressive changes in macroscopic shape.



By integrating experimental characterization with data-driven prediction, the framework enables prediction of complete three-dimensional degradation trajectories.

POSTER | SMART DATA ANALYSIS

POSTER 121 presented by:

NAME: Berta Tena

Characterization of blood pressure response during rehabilitation in individuals with spinal cord injury and stroke

Berta Tena[1], Mahtab Mohammadpoor Faskhodi[1], Inés Bueso-Inchausti[1], Daniel Romero[1,2,3],,, Jiaqi Wu[1], Anaïs Espinoso[4], Agustí Hernández[5], Yolanda Castillo-Escario[1,3], Raimon Jané[1,2,3]

[1] *Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain*
[2] *Universitat Politècnica de Catalunya-BarcelonaTech (UPC), Barcelona, Spain*
[3] *Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Barcelona, Spain*
[4] *NVISION Systems and Technologies S.L., Barcelona,Spain*
[5] *Fundació Institut Guttmann, Institut Universitari de Neurorrehabilitació, Badalona, Spain*

After a stroke (ST) or spinal cord injury (SCI), autonomic and cardiovascular regulation dysfunctions are very common. These alterations can affect how these individuals respond to changes in posture or exercise, which are common interventions during neurorehabilitation. The aim of this study is to characterize the blood pressure (BP) response during different rehabilitation protocols and to analyze the relationship between the observed patterns and clinical factors. Twenty participants were analyzed, 10 with ST and 10 with SCI, during two rehabilitation protocols: tilt-table sessions and seated cycling using a THERA-Trainer Tigo. In the tilt table protocol, the changes produced by a progressive increase in inclination were studied, while in the cycling protocol, the cardiovascular response to the effort required by exercise was analyzed. The BP and heart rate (HR) were continuously recorded with automated oscillometric upper-arm blood pressure monitor (ABPMpro) to study their evolution and behavior throughout the entire protocol.

Individuals showed heterogeneous BP responses during the tilt table protocol, both in ST and SCI, although greater individual variability was observed in SCI. HR progressively increased with inclination in both groups. Despite this heterogeneity, most individuals showed non-pathological responses. However, in some cases, decreases of >20 mmHg in BP were observed during changes in inclination, without adequate orthostatic compensation, reflected by a small increase in HR. This pattern is consistent with an altered cardiovascular response and may reflect impaired autonomic compensation mechanisms. During the cycling protocol, exercise produced a clear increase in HR in both groups, generally accompanied by an increase in BP. In both protocols, the results suggest that changes in the cardiovascular response are more evident in participants with SCI. On the other hand, severe patients showed a stronger BP response to changes in inclination, with a progressive decrease in systolic BP during the intermediate phases, while less dependent patients maintained more stable values. During cycling, the differences between severity levels were less marked, although individuals with greater dependency tended to show lower HR and more variable BP responses.

The results show a heterogeneous cardiovascular response during neurorehabilitation in individuals with ST and SCI. The differences observed according to neurological condition, functional severity, and other clinical factors such as medication, highlight the need to monitor and characterize the cardiovascular response continuously in order to prevent complications and optimize rehabilitation strategies.

Acknowledgements: This work is supported by the AURA project (MICIU/AEI CPP2022-009989)

POSTER 122 presented by:
NAME: Daniel Romero Perez

Assessment of Robust Cardiac Beat Detection Methods using Radar-based Physiological Signals

Daniel Romero[1,2,3], Mahtab Faskhodi[1], Yolanda Castillo-Escario [1,3], Anaïs Espinoso [4], Miquel Alfaras, Zouhair Haddi[4], Raimon Jané [1,2,3]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain
[2] Universitat Politècnica de Catalunya-BarcelonaTech (UPC), Barcelona, Spain
[3] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Barcelona, Spain
[4] NVISION Systems and Technologies S.L., Barcelona, Spain

Non-contact monitoring of vital signs has emerged as a promising alternative for applications where conventional contact-based sensors are impractical or uncomfortable, such as sleep monitoring, long-term home-based monitoring, and patient assessment in specific clinical conditions. This study compares two signal-processing approaches for the robust detection of cardiac fiducial points from non-contact radar signals recorded under resting conditions, using electrocardiogram (ECG) recordings as a reference.

First, the radar-derived distance signal was processed using a set of three bidirectional Butterworth bandpass filters with different cutoff-frequency combinations within the range 5–25 Hz. Second, variational mode decomposition (VMD) was applied to the 5– 25 Hz bandpass-filtered signals to obtain k non-overlapping narrowband mode components from the complex radar signal. Heartbeat detection was subsequently performed from the resulting Shannon energy-based envelope computed from the above signals. The accuracy of both approaches was assessed by comparing their obtained inter-beat interval (IBI) time-series with that one from the reference ECG using Pearson's correlation coefficient.

The results indicate that VMD provided good heartbeat detection performance and enabled reliable IBI time-series estimation, with r = 0.86. However, the bandpass-filtering approach achieved better temporal accuracy with substantially lower computational complexity, reaching r = 0.92. This result outperformed other methods based on heartsound-like signal analysis derived from the radar signal. These findings suggest that our approach could serve for further accurate HRV analysis, which depends on the reliable estimation of the IBI time series, beyond single average heart rates.

Acknowledgements This work was supported by the AURA project (MICIU/AEI CPP2022-009989).

POSTER | SMART DATA ANALYSIS

POSTER 123 presented by:

NAME: Giovanni Vito Spinelli

hpCSI: an open MATLAB toolbox for preclinical hyperpolarized ^{13}C spectroscopic imaging

Giovanni Vito Spinelli[1], Vicent Ribas Serra[1], Irene Marco-Rius[1]

[1] Molecular Imaging for Precision Medicine, Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain

Introduction. Hyperpolarized (HP) ^{13}C maps glycolytic flux in vivo, and the lactate-to-pyruvate ratio is an established metabolic biomarker in oncology [1]. Proton magnetic resonance spectroscopy is served by a mature ecosystem in which quantification packages are routinely benchmarked against one another [2]. HP ^{13}C has no equivalent, largely for a physical reason: the magnetization is created once and consumed by every excitation, so signal amplitude reflects polarization and pulse history rather than concentration [3], and the basis-set quantification underlying conventional MRS software does not apply. Two open-source frameworks are established, the hyperpolarized MRI toolbox [4] and SIVIC [5], but neither covers the preclinical route from raw spectra through grid-to-anatomy registration to zone-resolved analysis. Here we present hpCSI, a modular MATLAB toolbox for this workflow, demonstrated in a mouse model of glioblastoma (GBM).

Methods. Data were acquired on a Bruker BioSpec 3T preclinical scanner in female C57BL/6J mice bearing in-tracranial SB28 glioma, imaged at day 11–12 post-inoculation. Two-dimensional ^{13}C CSI used a 16 × 16 matrix over a 37.0 × 30.5 mm field of view (2.31 × 1.91 mm in-plane, 3.5 mm slice), TR/TE 349/1.2 ms, 22° excitation and 1024 spectral points across 100.8 ppm centred at 170 ppm, following intravenous injection of hyperpolarized [1-^{13}C]pyruvate prepared by dissolution DNP. Two T2-weighted RARE images were acquired, one matched to the CSI geometry and one with enlarged field of view for display. In hpCSI, FIDs are apodized and echo-shifted, and zero- and first-order phase are corrected automatically by negative-lobe and entropy minimization respectively [6], with per-voxel manual override. Pyruvate and lactate areas are integrated over user-defined windows (169–172 and 182–185 ppm) after en-forcing ascending chemical-shift order, so a negative area flags a phase error instead of being masked by the modulus. The spectroscopic grid is placed on the anatomical image directly from the acquisition parameters. Both grids share the field-of-view centre but differ in element size, so the first metabolic voxel sits inward of the first anatomical pixel by half that difference; the offset $S = (\Delta pix - \Delta vox)/2$ is applied as a fixed correction. Tumour boundaries are outlined on T2, refined by an edge-based active contour, and CSI voxels assigned to the tumour zone by area fraction.

Results and Discussion. hpCSI processed the GBM dataset end to end, from raw spectra to a segmented metabolic map, with no manual alignment at any stage. The geometric correction shifts the spectroscopic grid by [Sx] and [Sy] mm, close to half a CSI voxel in each direction, which at 2.31 × 1.91 mm moves the tumour boundary by a full voxel (Fig. 1a). The edge-based contour tracks the hypointense rim, where a region-based formulation has no intensity difference to act on, and the Lac/Pyr map shows elevated ratio containing the segmented lesion and extending beyond it, consistent with the point spread function at this

resolution (Fig. 1b). hpCSI is in internal use, with release as a standalone executable planned. The pipeline has also been applied successfully to a hepatic dataset, which will be presented as a second application.

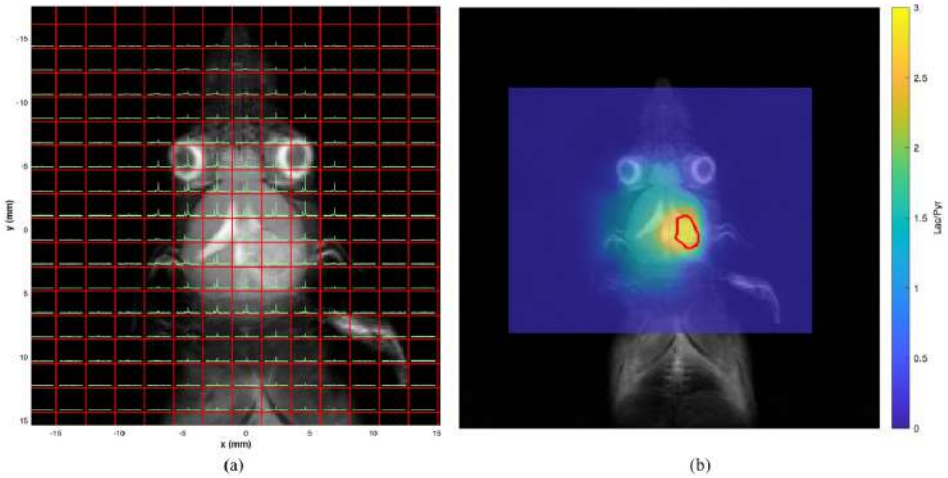


Figure 1: hpCSI applied to a murine GBM dataset. (a) ^{13}C spectra overlaid on the T2 reference after geometric correction, with the CSI grid in red. (b) Interpolated Lac/Pyr map over the T2 with the tumour segmentation contour in red.

RMIneatfgJenrBeRnieocsmeosen.dM[l1me]daP.gai2rnk0g2.l4,2;e90t11(3a6;l)2.:02N123e0:u41r–6o2925O228n6..co[[l64.]]2CL0ah1re0sn;o1n2L(,P2W)E:1eZ3n,3ge–tZ14,a4lG..o[hh2y]pLCe,rrGpaoavlrealnarinAzdeRdM-,me. trJia-tMlo. oaNlgbnMoxRR.eBsdooinoi:.m102e.0d50.2282;110/52z82e(;n315o–(2d7)o):.1:1e614497–8019261.85.[.3][5L]aCrsroannePJECZ,, eett aall..

POSTER | SMART DATA ANALYSIS

POSTER 124 presented by:

NAME: Inés Bueso

Development of an Integrated Application for Automatic Data Acquisition and Transmission in Sleep Apnea Monitoring

I. Bueso-Inchausti[1], Y. Castillo-Escario[1,2,3], R. Jané[1,2,3]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology, Barcelona, Spain
[2] Universitat Politècnica de Catalunya - BarcelonaTech (UPC), Barcelona, Spain
[3] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Spain

Sleep apnea is a disorder characterized by recurrent pauses or reductions in airflow during sleep, leading to sleep fragmentation and serious health consequences. Despite its high prevalence, sleep apnea remains largely underdiagnosed, while conventional diagnostic approaches still present important limitations.

Digital tools have opened new possibilities for simpler, cost-effective, and unobtrusive monitoring, with mHealth tools emerging as a promising alternative. Our team introduced a mHealth system for sleep apnea monitoring that combines smartphone sensors (microphone and accelerometer) and a pulse oximeter for multimodal data acquisition. The system was validated against gold-standard devices, demonstrating comparable performance[1,2].

This work integrates the system into an Android-based application to streamline data acquisition and transmission through a unified workflow, enabling secure data transfer to a cloud repository for remote monitoring and data management. It integrates the smartphone's built-in accelerometer, audio recordings, and a Bluetooth-connected pulse oximeter for physiological signal collection, with Automate supporting process automation. The application provides an intuitive user interface with two defined options: data acquisition and data transmission, both largely automated and requiring minimal user intervention. The acquisition option initiates signal recording and device configuration, while transmission requires only PIN authentication and pulse oximeter pairing, with notifications and alerts managed automatically. An initial validation study was conducted at Vall d'Hebron Hospital, successfully acquiring and uploading 80 sleep recordings from patients with suspected sleep apnea.

Overall, this work presents a novel Android-based solution that integrates and automates physiological signal management into an intuitive platform for sleep apnea monitoring.

Acknowledges: This work was supported by AGAUR PRODUCTE-IdC program (2025PROD00139), by Fundació La Marató de TV3 (202533-30-31), and by MICIU/AEI/FEDER (PID2024-160620OB-I00).

References

[1] Castillo-Escario Y, Ferrer-Lluis I, Montserrat JM, Jané R. Entropy analysis of acoustic signals recorded with a smartphone for detecting apneas and hypopneas: a comparison with a commercial system for home sleep apnea diagnosis. IEEE Access, vol 7, 2019, pp. 128224 [2] doi:10.1109/access.2020.2987153

[2] Ferrer-Lluis I, Castillo-Escario Y, Montserrat JM, Jané R. Analysis of Smartphone Triaxial Accelerometry for Monitoring Sleep-Disordered Breathing and Sleep Position at Home. IEEE Access, vol 8, 2020, pp. 71231-71244

POSTER 125 presented by:
NAME: Jaime Casado García-Consuegra

Spatial tracking of clonal evolution reveals genetic and chemotherapeutic dynamics in Small Cell Lung Cancer

Jaime Casado García-Consuegra[1,2,5], Alexandros Drainas[3,5], Antonio Delgado-González[3], Theresa P. Chu[4], Yunhao Bai[4], Garry Nolan[4], Julien Sage[3*], Xavier Rovira-Clavé[1,4*]*

Understanding how cancer cell subclones adapt to the changing tumor microenvironment is key to designing successful cancer therapies. Despite recent breakthroughs in transcriptomic profiling and our understanding of phenotypic plasticity, it remains unclear how specific genetic alterations and therapy exposure influence subclonal evolution and the spatial organization or interactions of distinct tumor subclones within the tumor microenvironment. In this context, combinatorial tagging combined with spatial omics readouts to track barcodes in situ within tissue samples allow 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. Here, we integrated a protein-based barcoding approach with CRISPR-mediated perturbation of candidate cancer genes and cisplatin treatment in a small cell lung cancer xenograft model to spatially resolve how genetic and chemotherapeutic pressures influence clonal dynamics and tumor architecture. We observed that knocking out specific 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, cells lacking NF2, a tumor suppressor involved in contact inhibition, showed enhanced expansion. Under cisplatin treatment, SLFN11 knockouts, known to mediate sensitivity to DNA-damaging agents, expanded preferentially. We observed spatially organized clonal patches, defined by the local enrichment of cells sharing the same genetic subclone across treatment-exposed and phenotypically distinct tumor regions, with patch dispersion, size, and phenotypic composition varying across subclones and treatment conditions. Furthermore, our results revealed diverse interactions between clones under different treatment conditions, including preferential associations between ROBO1- and CADM1-deficient clones in untreated tumors and between NOTCH2- and REST-deficient clones following cisplatin treatment, 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 spatial barcoding approach in providing new perspectives on the processes driving tumor growth and therapeutic resistance, offering valuable insights for the advancement of personalized cancer treatments.

POSTER | SMART DATA ANALYSIS

POSTER 126 presented by:

NAME: Jaume Rodríguez Soler

Artificial intelligence for the classification of obstructive and central sleep apnea using triaxial accelerometery

Jaume Rodríguez Soler[1], Yolanda Castillo-Escario[1,2], Raimon Jané[1,2,3]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), 08028 Barcelona, Spain
[2] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), 28029 Madrid, Spain
[3] Universitat Politècnica de Catalunya-Barcelona Tech, 08028 Barcelona, Spain

Sleep apnea (SA) is a breathing disorder characterized by the reduction or cessation of airflow during sleep. SA can be subclassified into obstructive sleep apnea (OSA) and central sleep apnea (CSA) based on their underlying mechanism. SA is a risk factor for cardivoascular diseases, but it remains largely undiagnosed in the general population. Polysomnography is the gold-standard diagnostic technique, but it requires clinical supervision, specialised rooms, expensive equipment and manual annotation of overnight recordings, thus being a non-viable option for large-scale diagnosis. Triaxial accelerometery and audio signals recorded by smartphones have been successfully proposed for SA diagnosis in a reduced setup as a digital health solution [1]. In this work, we focus on the ability to classify between OSA and CSA using only accelerometer data. Supervised Vector Machine (SVM), Random Forests (RFs) and Convolutional Neural networks (CNN) were trained to classify the two classes. Very good results were obtained with all models, with the best results obtained with CNN (AUC=98.8%). Robust results were also obtained from the feature-based classifiers, SVM (AUC=94.5%) and RF (AUC=97.3%), which can facilitate the understanding of SA characteristics. Furthermore, their easier interpretability can be an advantage for a fast clinical adoption. Artificial Intelligence applied to accelerometery recordings shows a great potential for SA classification.

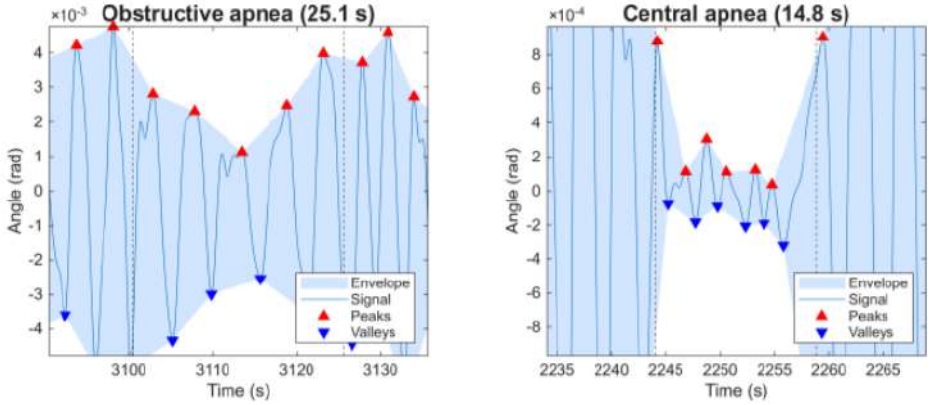


Figure 1. Example of Obstructive and Central Sleep apnea from processed tri-axial accelerometery

Acknowledgements: This work was supported by AGAUR PRODUCTE-IdC program (2025PROD00139), by Fundació La Marató de TV3 (202533-30-31), and by MICIU/AEI/FEDER (PID2024-160620OB-I00).

References

1. I. Ferrer-Lluis, Y. Castillo-Escario, J. M. Montserrat, and R. Jane, "Analysis of Smartphone Triaxial Accelerometry for Monitoring Sleep-Disordered Breathing and Sleep Position at Home," *IEEE Access*, vol. 8, pp. 71231–71244, 2020, doi: 10.1109/access.2020.2987488.

POSTER 127 presented by:

NAME: Mahtab Mohammadpoor Faskhodi

Assessment of Radar-Based Contactless Respiration Monitoring in Individuals with Stroke and Spinal Cord Injury

Mahtab Mohammadpoor Faskhodi[1], Berta Tena[1], Daniel Romero [1,2,3], Jiaqi Wu [1], Anaïs Espinoso [4], Agustí Hernández [5], Yolanda Castillo-Escario [1,3], Raimon Jané [1,2,3]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona, Spain
[2] Universitat Politècnica de Catalunya-BarcelonaTech (UPC), Barcelona, Spain
[3] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Barcelona, Spain
[4] NVISION Systems and Technologies S.L., Barcelona, Spain
[5] Fundació Institut Guttmann, Institut Universitari de Neurorrehabilitació, Badalona, Spain

Radar-based contactless sensing has emerged as a promising approach to unobtrusive respiratory monitoring, enabling the detection of chest-wall displacements associated with breathing activity. Such advantages are especially relevant in neurorehabilitation, where individuals with stroke or spinal cord injury (SCI) may experience autonomic and cardiorespiratory dysfunctions that require continuous physiological monitoring to prevent complications and support the optimization of therapy.

Among the radar technologies suitable for respiratory monitoring, Continuous-Wave (CW) radar offers a simple architecture while providing sufficient sensitivity to detect the small chest-wall movements associated with respiration. Accordingly, this study employed a 24 GHz CW radar system (Sykno ViRa24) for non-contact respiratory monitoring. The received RF signal contains subtle respiratory variations together with environmental interference and other sources of signal disturbance, making the reliable extraction of respiratory information challenging. Consequently, appropriate signal-processing methods are essential to enhance the quality of the extracted respiratory signals and improve the reliability of respiratory-rate estimation.

In this study, the radar system was used for continuous, non-contact monitoring of respiration in individuals undergoing neurorehabilitation. The study included ten individuals with stroke and ten individuals with SCI. Radar-based respiration measurements were assessed in two rehabilitation contexts: (1) tilt-table sessions and (2) seated cycling (THERA-Trainer tigo). These conditions were selected to evaluate the performance of radar-based respiratory monitoring across different body postures and levels of physical activity. The radar-derived respiratory measurements were evaluated by comparison with respiration signals obtained from the Bionomadix wearable reference system. The correlation between the radar-based measurements and the reference respiration signals was greater than 95% during tilt-table sessions and greater than 90% during cycling. These results indicate a high level of agreement between the contactless radar measurements and the reference system across both rehabilitation conditions. Due to the obtained result, CW radar shows promise as an accurate, unobtrusive tool for continuous respiratory monitoring in neurorehabilitation.

Acknowledgements

This work was supported by the AURA project (MICIU/AEI CPP2022-009989).

POSTER | SMART DATA ANALYSIS

POSTER 128 presented by:

NAME: Renato Eduardo Yanac Huertas

AnalyCa: a code-free calcium imaging tool, benchmarked in a tauopathy neuronal model

Renato Eduardo Yanac-Huertas[1,2], Neus Gil-Sancho[2], Miriam Segura-Feliu[2], Karolina Zimkowska[2], Marc Riu-Villanueva[2], Romen Rodriguez[1,2], Oscar Castaño[1,2], José Antonio Del Río[2]

[1] Electronics and Biomedical Engineering, Universitat de Barcelona, Barcelona, Spain
[2] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST), Science Park of Barcelona, 08028 Barcelona, Spain.

Calcium imaging analysis often requires scripting skills, dedicated software environments, or complex software installation. While several powerful tools are available, accessibility remains a major barrier for many users. AnalyCa was developed to provide a code-free workflow for calcium imaging analysis while maintaining analytical reliability. AnalyCa a code-free desktop application (Windows/macOS) that integrates ROI selection, signal processing, event detection, and network analysis into a unified graphical workflow that requires no programming experience. Published and validated analysis components were integrated into a unified graphical workflow; while numerical processing is executed through a MATLAB engine in the background.

To assess whether improved accessibility compromises analytical performance, AnalyCa was benchmarked against FluoroSNNAP in a neuronal tauopathy model. Mouse cortical cultures in microfluidic devices received AAV-delivered GCaMP6s alone, or with mouse 2N4R or human P301L tau, and spontaneous activity was imaged at 14 days in vitro. Fifteen recordings were processed twice, once with AnalyCa (930 manually selected neurons) and once with FluoroSNNAP under its own automatic segmentation (1,092 neurons). At the single-cell level, 12 of 15 predefined contrasts met equivalence criteria (±2-fold margin); three were inconclusive, none showed disagreement. At the population level, 7 of 15 were equivalent; three differed due to distinct population signal construction methods.

Agreement was level dependent. At the single-cell level, 12 of 15 predefined contrasts met equivalence criteria, while the remaining three were inconclusive and none indicated disagreement between platforms. At the population level 7 of 15 were equivalent and 3 differed, because the two pipelines build their population signals differently. These results indicate that AnalyCa can reproduce most biologically relevant conclusions obtained with an established analysis platform while substantially lowering the technical barrier for calcium imaging studies.

Acknowledgements

We acknowledge financial support from grants PID2021-124575OB-I00 and PID2024-159777OB-I00, funded by MICIU/AEI/10.13039/501100011033. We also acknowledge

funding from Torró Solidari (Torrons Vicens-RAC1).

POSTER 129 presented by:
NAME: Valentina Schastlivaia

Topology-driven modeling of LRP1-mediated of BBB-crossing nanomedicines: replacing discrete receptor sites counting with surface tension field on homeomorphic manifolds

Schastlivaia V.[1,2], Battaglia G.[1,3]

[1] The Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology (BIST)
[2] BarcelonaTech (UPC), Applied Mathematics Doctoral Programme
[3] The Catalan Institution for Research and Advanced Studies (ICREA)

Receptor-mediated transcytosis through LRP1 is a leading route for delivering nanoparticle (NP) therapeutics across the blood–brain barrier (BBB), and specific-ligand-functionalized NPs exploit this pathway. Quantitative models of NP avidity, however, hinge on the number of receptor binding sites - a quantity that is ambiguously defined for LRP1: depending on the contact cutoU, molecular docking assigns between 9 (major interactive motifs) and 27 binding sites, injecting large uncertainty into any discrete, combinatorial-entropy estimate of binding free energy.

We remove this bottleneck by recasting binding as a continuous energy-field problem. The LRP1 receptor is represented by a smooth surface that is topologically homeomorphic to the receptor, preserving its genus and multi-lobe structure, so that binding is governed by intrinsic geometry rather than enumerated motifs. A surface-tension field defined from molecular docking and the Gaussian curvature localizes aUinity. Single-ligand binding energy is computed as a high-order surface integral of this field within an interaction shell; the NP–cell binding free energy then follows as a Boltzmann-weighted volume integral over all possible NP positions in the binding volume. The approach incorporates ligand density for estimation of ligand availability for multivalent binding, PEG-brush entropic-spring repulsion, and glycocalyx (GAG) steric penalties.

The result is a continuum partition-function model of nanoparticle–receptor binding via surface and volume integrals of an interaction field. We present binding-energy landscapes for specifically functionalized NPs against an LRP1-homeomorphic surface that enables the rational design of BBB-crossing nanomedicine.

POSTER | SMART DATA ANALYSIS

POSTER 130 presented by:

NAME: Yolanda Castillo Escario

Assessment of Night-to-Night Variability in Sleep Apnea using Smartphone-based Sensing and Multimodal Biomarkers

Yolanda Castillo-Escario[1,2], Inés Bueso-Inchausti[1], Raimon Jané[1,2,3]

[1] Institute for Bioengineering of Catalonia (IBEC), Barcelona Institute of Science and Technology, Barcelona, Spain
[2] Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Madrid, Spain
[3] Universitat Politècnica de Catalunya - BarcelonaTech (UPC), Barcelona, Spain

Sleep apnea is one of the most common sleep disorders. Although there is substantial night-to-night variability (NtNV) in sleep apnea metrics, the diagnosis still relies on a single night and classical parameters like the apnea-hypopnea index (AHI). Home sleep studies with portable simplified systems, including smartphone-based sensing, can facilitate longitudinal monitoring and multimodal multi-night assessment of sleep apnea, for more accurate evaluation and risk stratification. This study proposes a smartphonebased system to investigate NtNV in the AHI and additional sleep parameters.

A novel smartphone-based system was used to conduct home sleep tests during three nights in thirty-two volunteers, recording overnight audio, accelerometer, and pulse oximetry data. These signals were analyzed with automatic custom-made algorithms to extract clinical indices and novel multimodal digital biomarkers. We quantified NtNV in AHI and hypoxic burden (HB) and studied their relationship with other sleep parameters related to oxygenation, sleep position, nocturnal body movements, and breathing route (nasal vs oral).

Our results indicate that there was high NtNV in AHI, with a median within-subject range of 6 events/h (Q1-Q3: 3-10) and coefficient of variation (CV) of 22% (13-31), resulting in changes in severity level between nights in half of participants. HB also showed considerable NtNV, although slightly lower than AHI, with a CV of 15% (11-22). HB and AHI showed an approximately linear relationship at lower severity levels (R^2=0.76 for AHI<15 events/h), which became more dispersed at higher AHI values (R^2=0.26). Nightto-night differences in AHI were associated with increases in supine time (p=0.02) and oral breathing (p=0.03).

This study provides a smartphone-based system for multi-night sleep apnea assessment and a multimodal approach to quantify NtNV. Our findings highlight the impact of NtNV on sleep apnea diagnosis and the risk of incorrect stratification using only one night measurements, supporting the value of multi-night studies and multimodal digital biomarkers beyond the AHI for more accurate and accessible patient monitoring.

Acknowledgements: This work was supported by Fundació La Marató de 3Cat (202533-30-31), by MICIU/AEI/FEDER (PID2024-160620OB-I00), and by AGAUR PRODUCTE-IdC (2025PROD00139).

POSTER 131 presented by:
NAME: Sustainability Committee

Building a Culture of Sustainable Science at IBEC: From Green Labs to Institutional Transformation

Sustainability has become a strategic priority at the Institute for Bioengineering of Catalonia (IBEC), driving a progressive transformation of research and research management practices. Since 2019, IBEC has developed a comprehensive sustainability roadmap that combines institutional commitment, operational improvements, community engagement, and continuous monitoring. Key milestones include the creation of the IBEC Sustainability Committee in 2020, the publication of the institute's sustainability strategy in 2021, the integration of sustainability into the 2023-2026 Strategic Plan, the implementation of a Research Management Sustainability Plan in 2026, and successive rounds of My Green Lab certification.

Actions implemented at IBEC span multiple areas, including energy and water conservation, waste reduction, sustainable purchasing, mobility, training, awareness raising, and participation in sustainability networks. Initiatives such as sustainable procurement measures, reuse and donation programs for laboratory materials, sustainable mobility campaigns, and communication activities have helped embed sustainability into everyday practices across the institution.

These efforts have been supported by a strong governance framework, measurable indicators, and active engagement from researchers, technicians, and research management staff. IBEC's leadership in sustainable research has gained international recognition, including coverage in Nature Physics, highlighting the institute's efforts to reduce the environmental impact of scientific research while maintaining excellence and innovation.

IBEC's journey shows that sustainability is not an add-on to scientific excellence, but a driver of innovation, efficiency, and institutional transformation.

POSTER | ADDITIONAL POSTERS

POSTER 132 presented by:

NAME: Fátima Serrano

MicroFabSpace: Enriching Core Facilities to Support IBEC Research

Fátima Serrano[1], Sandra Segura[1], Teresa Galán[1]

[1] MicroFabSpace Facility – Core Facilities Unit – Institute for Bioengineering of Catalonia, Barcelona, Spain

The MicroFabSpace is the IBEC's microfabrication facility, serving as a bridge between innovative research concepts and their experimental implementation. With a strong commitment to supporting scientific advancement, the facility continuously expands its technological capabilities to address emerging research needs and provide state-of-the-art fabrication solutions to the research community.

Over the last year, several strategic developments have been implemented to enhance the facility's services and broaden its technological portfolio. Among the most significant advances are improvements in replication methodologies, additive manufacturing capabilities, lithographic resources, and characterization infrastructure.

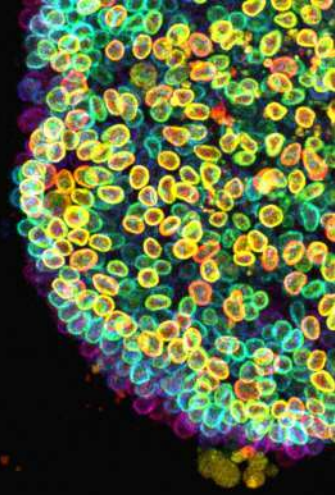
A new methodology has been established for the replication of PDMS molds into rigid resin masters, enabling efficient master reproduction while reducing dependence on the original molds. The resulting resin masters were demonstrated to be compatible with further replication processes for microfluidic device fabrication.

In addition, new objectives have been incorporated into the two-photon polymerization (2PP) system, significantly improving fabrication throughput and extending the printable size range. Preliminary work has also been initiated on the processing of bioinks and custom materials for 2PP, offering researchers increased flexibility for the development of advanced applications.

To strengthen in-house lithographic capabilities, a new acetate mask manufacturing system has been acquired and is currently being optimized, providing a cost-effective and rapid alternative for mask fabrication.

Furthermore, the facility has expanded its characterization infrastructure with the installation of a new sputter coating system for SEM sample preparation. Located within the SEM laboratory and designed for autonomous operation, this equipment increases user independence and facilitates experimental planning.

Through these continuous improvements, the MicroFabSpace aims to streamline research workflows, expand technological opportunities, and foster innovation across the institute while remaining responsive to the evolving needs of its users.



20 YEARS IBEC

Institute for Bioengineering of Catalonia

Baldiri Reixac, 10-12
08028 Barcelona, Spain
Tel. +34 934 039 706

www.ibecbarcelona.eu

CERCA Research Centres of Catalonia

Excelencia Severo Ochoa

bist

Universitat de Barcelona

Universitat Politècnica de Catalunya BarcelonaTech

Generalitat de Catalunya Departament de Salut

Generalitat de Catalunya Departament de Recerca i Universitats

Image credit: Özge Özgüç, Integrative Cell and Tissue Dynamics Research Group.