18th PhD meeting

TECSBI

2026

BOOK OF ABSTRACTS

22-24 **SETTEMBRE**

OSTELLO MONTEBARRO

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

BtBs Department of Biotechnology and Biosciences

SCUOLA DI DOTTORATO BICOCCA

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Converging Technologies for Biomolecular Systems (TeCSBI)

18th PhD Meeting - 22/24 September 2026
Località Eremo di Monte Barro, via Balassi, Galbiate (LC)

Speakers

S1.

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Characterizing Cellular Metabolism via Flux Enrichment Scores: A Versatile Framework for Bulk, Single-Cell, and Spatial Transcriptomics

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CELLULAR METABOLISM, TRANSCRIPTOMICS, CANCER METABOLISM, EMBRYONIC DEVELOPMENT

Metabolic reprogramming is a key indicator of cellular state across biological processes. We present a computational framework integrating transcriptomics, either bulk, single-cell, or spatial, onto curated human metabolic networks. Using Reaction Activity Scores and flux sampling, our method generates Flux Enrichment Scores (FES), enabling functional characterization and comparison of metabolic activity across conditions, cell types, or tissue regions. A central component is spatial Flux Balance Analysis (spFBA), revealing region-specific metabolic rewiring and niche heterogeneity within tissue architecture, uncovering localized metabolic programs and nutrient exchange patterns invisible to gene expression alone. We demonstrate the framework potentiality across applications spanning cancer and embryonic development, and its potential integration into machine learning pipelines to identify non-metabolic transcriptional predictors of metabolic activity.

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Mirror-Image Peptide Nanoparticles Improve Nucleic Acid Protection, Intracellular Delivery, and Innate Immune Activation

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PEPTIDE NANOPARTICLES, NUCLEIC ACID DELIVERY, MIRROR-IMAGE PEPTIDES, MICROFLUIDIC, ENDOSOMAL ESCAPE

Peptide-based nanoparticles are promising carriers for therapeutic nucleic acid delivery, yet their broader translation remains limited by poor biological stability, sensitivity to proteolytic degradation, and variable manufacturing reproducibility. Here, we present a strategy to address these challenges by combining chemical peptide engineering with automated manufacturing approaches. We developed a nanoplatform based on an amphipathic peptide composed entirely of D-amino acids, named Mirror-Image-RALA and benchmarked it against its parental analogue RALA for the delivery of several nucleic acid cargoes. Using microfluidic technology, we produced highly reproducible nanoparticles with controlled physicochemical properties across siRNA, mRNA, and DNA-based payloads.

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Spectroscopic approaches for the identification of biomolecular signatures of ageing and age-related processes

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NMR, METABOLOMICS, BIOSTATISTICS, NATURAL EXTRACTS, BIOMOLECULES, AMYLOID-B

Investigating With the progressive increase in life expectancy, age-related pathologies, which are closely linked to age-associated processes such as immunosenescence [1], are becoming a major public health challenge [2], highlighting the need for reliable diagnostic and prognostic tools for the early identification and monitoring of ageing-associated functional and cognitive decline. The first work package of the project focuses on the NMR-based metabolomic profiling of plasma samples collected within the multicentric IN-TeMPO trial [3]. Metabolic profiles have been integrated with clinical, functional and demographic data through multivariate statistical analyses to identify biomarkers associated with ageing and the effect of multicomponent interventions. The second work package investigates natural extracts as sources of anti-amyloidogenic compounds [4-6]. Myrtle leaves extracts have been characterized by NMR and LC-HRMS to identify compounds with potential neuroprotective activity.

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A milli-fluidic 3D co-culture system for characterizing microenvironment driven therapy resistance mechanisms in esophageal adenocarcinoma

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EESOPHAGEAL ADENOCARCINOMA, STROMAL CO-CULTURE SPHEROIDS, 5-ELUOROURACIL RESISTANCE, MILLIFLUIDIC PLATFORM, DYNAMIC FLOW

Stroma plays a critical role in esophageal adenocarcinoma (EAC) progression and therapy resistance. We developed a co-cultured spheroid-based EAC model and incorporated it within the MIVO® millifluidic platform to study stromal interactions and recapitulate therapy resistance under dynamic flow. OE33 wild-type (WT) cell line and its 5-fluorouracil-resistant counterpart (5FU-R) were used to form spheroids alone or with CCD-1132Sk fibroblasts (2:1, 5:1, 10:1 ratios). WT cells formed stable, compact spheroids within 2 days, while 5FU-R cells formed loosely compact aggregates only after 7 days. Under dynamic flow (0.07 mL/min) in the MIVO chamber for up to 5 days, WT spheroids remained stable and viable, whereas 5FU-R spheroids lost structural integrity within 2 days, suggesting a possible mesenchymal phenotype shift in resistant cells. Future work will include characterization using immunohistochemistry and recapitulating EAC-specific chemo and immunotherapy for functional analysis.

* To attend these sessions, participants are required to sign a confidentiality agreement to ensure that all research presented remains protected and is not shared without authorization

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NMR spectroscopy as a red thread in the study of biomolecular interactions: from bacterial recognition to amyloid aggregation

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NMR SPECTROSCOPY, BIOMOLECULES, BACTERIA, AMYLOID PROTEINS, AB1-42

Biomolecular interactions play a central role in all life events by orchestrating both cellular and extra-cellular processes. [1] Thus, their structural characterization is crucial to unravel the underlying molecular mechanisms of key biological pathways and to harness their properties for biotechnological purposes. In this context, Nuclear Magnetic Resonance (NMR) spectroscopy has found wide application due to its ability to study highly dynamic and heterogeneous complexes in a robust, quick, and accurate manner. [2]

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Wild bees in the Anthropocene: eco-evolutionary trajectories

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BEES, ANTHROPOCENE, EVOLUTIONARY ECOLOGY

Industrialization, urbanization, and agricultural intensification stand as principal anthropogenic forces driving the ongoing global loss of pollinator biodiversity. Yet these changes do more than erode species richness since they impose selective pressures that may reshape organisms' traits and reroute their evolutionary routes. Integrating population ecology and genomics, we can distinguish plastic phenotypic adjustments from adaptive genetic responses, assess population viability. Beyond providing an historical reconstruction, this integrative approach is essential for assessing population viability and for providing conservation strategies. Focusing on human-altered landscapes, we examine three axes in bees: pathogen spillover, metabolic remodeling, and demographic drivers. The main results show how even populations of species classified by IUCN as Least Concern are in decline, highlighting the urgent need to update conservation monitoring strategies with novel genomic-based tools.

s7.

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Decoding HSC identity: a single cell multiomics approach to dissect Hematopoietic Stem Cell heterogeneity

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HEMATOPOIETIC STEM CELLS, BIOINFORMATICS, GENE THERAPY, HUMAN BIOLOGY

Hematopoietic Stem Cells (HSCs) are central to advanced therapies for blood and immune disorders. Despite their clinical importance, their functional potential remains difficult to predict, as traditional markers like CD34+ expression often fail to capture true stem cell identity. Furthermore, the "CLOUD" of low-primed undifferentiated hematopoietic cells appears too uniform in standard transcriptomics to reveal their distinct identities.
To address this, we developed a bioinformatics single-cell multi-omics workflow that integrates gene expression and chromatin accessibility. By coupling this computational framework with lab-developed HSC expansion strategies, we show that epigenetic regulation, rather than transcriptomics alone, defines the primitive HSC compartment. Our approach identifies discrete functional states, offering a robust tool to characterize HSC therapies. Future work will integrate clonal tracking via lentiviral barcoding to refine predictions of in vivo engraftment.

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Microbial adhesion promotes Piezo1 activation to initiate innate immunity

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INFECTION, INNATE IMMUNITY, PIEZO1, MECHANOSENSING, NEUTROPHILS

How mammals mount an effective immune response against infectious agents remains unresolved. Here, we identify microbial adhesion to myeloid cells as a critical initiating event that precedes Pattern Recognition receptor (PRR) engagement. Using a skin infection model with pathogenic bacteria and fungi, we demonstrate that neutrophil recruitment occurs in two sequential phases. The early phase is PRR-independent and instead driven by microbial adhesion, which engages the mechanosensitive ion channel Piezo1 to promote leukotriene (LT)B4 production. Together with interleukin 1α, LTB4 induces CXCL1 release, triggering neutrophil infiltration via the same circuit at play during sterile inflammation. In contrast, the late phase is Toll like Receptor- and CXCL2-dependent, marking a transition to the canonical, pathogen-driven response. Our findings uncover microbial adhesion as a previously unrecognized danger signal that activates innate immunity via mechanotransduction.

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Modelling a TARDBP-ALS Family in iPSC-Derived Neural Stem Cells Uncovers Proliferative and Metabolic Defects

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ALS, TDP-43, HINSCS, PROLIFERATION, METABOLISM

Amyotrophic lateral sclerosis(ALS) is a fatal neurodegenerative disease characterized by progressive motor neurons degeneration, paralysis and death. TARDBP mutations account for 4% of familial ALS cases (fALS), but pathogenic mechanisms remain still unclear.
We are now exploring the molecular mechanisms underlying this synthetic lethality, in particular we are analysing the role of polymerases and nucleotides to better figure out how the CIA system can modulate the cellular response to DNA damage.

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Enzyme-mediated tuning of cellulose surface reactivity for innovative compounding purposes

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BACTERIAL CELLULOSE, POLYMERS FUNCTIONALIZATION, INULIN, PROTEIN ENGINEERING

Bacterial cellulose (BC) features high purity and versatile applications, making its modification crucial for properties tuning. This study focuses first on optimizing BC production by varying the carbon substrates in the culture medium of the bacterium Komagataeibacter sucrofermentans. The highest titer was achieved using inulin, a food industry byproduct, with a SHF or SSF processes. The BC was then functionalized via two strategies: ex situ through lipase-mediated catalysis, and in situ via the incorporation of N-acetylglucosamine (NAG) monomers. To tailor the in situ approach, chitin deacetylase (CDA) was utilised to modify NAG. To optimize the efficiency of synthesis reaction, CDA performance is currently being enhanced using two parallel protein engineering approaches: rational design and machine learning. The results demonstrate the viability of utilizing industrial waste for BC synthesis and while establishing new avenues for the biocatalytic tailoring of advanced biomaterials.

* To attend these sessions, participants are required to sign a confidentiality agreement to ensure that all research presented remains protected and is not shared without authorization

S11.

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Exploring the Postbiotic Potential of Zygosaccharomyces bailii KAV1 isolated from Kombucha

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POSTBIOTIC, YEAST, KOMBUCHA, EXOPOLYSACCHARIDES

Postbiotics are promising alternatives to live microorganisms, but scientific research has mostly focused on bacteria, leaving the potential of yeasts underexplored. This study evaluated the postbiotic potential of Zygosaccharomyces bailii KAV1, a kombucha-derived yeast, characterizing its antioxidant, immunomodulatory and barrier-supporting effects. Z. bailii KAV1 supernatants analysis by GC–MS revealed the presence of bioactive metabolites, including branched-chain fatty acids, and phenylethyl alcohol. Upon DPPH, PBMCs and TEER tests of the supernatants, enhanced antioxidant activity, reduced IFNγ^{+} CD4^{+} T cells, improvement of TEER after inflammatory challenge were shown along with a selective boost of the probiotic strain Lactobacillus rhamnosus APC228. Interestingly, Z. bailii KAV1 was shown to produce exopolysaccharides (EPS), that were chemically and biologically characterized. Overall, KAV1 represents a promising non-conventional source of postbiotic metabolites and EPS.

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A DIAPH1-SOWAHC-CFL1 Axis Regulates Macropinocytosis and Chemoresistance in Cervical Cancer

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DIAPH1, SOWAHC, ADF/COFILIN, MACROPINOCYTOSIS, CERVICAL CANCER

Formin mDia1 (DIAPH1) regulates actin dynamics, cell migration and membrane remodeling, processes often dysregulated in cancer. Here, we identify a DIAPH1-dependent signaling axis controlling macropinocytosis and cisplatin sensitivity in cervical cancer. Label-free quantitative mass spectrometry in DIAPH1 knockout HeLa cells identified SOWAHC as a novel DIAPH1 interactor, validated by reciprocal co-immunoprecipitation. Loss of DIAPH1 or SOWAHC increased cofilin (CFL1) phosphorylation, indicating reduced CFL1 activity. DIAPH1, but not SOWAHC, was required for EGF-induced ruffling and random migration, whereas macropinocytosis was impaired in both knockout models, revealing a selective role for SOWAHC in uptake. DIAPH1 loss also sensitized HeLa cells to cisplatin. In 322 cervical cancer cases, DIAPH1 and SOWAHC were elevated and inversely correlated with phospho-CFL1. These findings define a DIAPH1-SOWAHC-CFL1 axis linking actin remodeling, macropinocytosis and drug response.

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A natural compound counteracts metabolic associated fatty liver disease by stimulating lipolysis and lipophagy and promoting β-oxidation

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MAFLD, NATURAL COMPOUNDS, AMPK-PKA PATHWAY, HEPG2 CELLS, DROSOPHILA MELANOGASTER

Targeting metabolic pathways via bioactive molecules is a promising strategy to reverse early-stage MAFLD, characterized by hepatic lipid accumulation(1,2). We investigated the metabolic effects of a natural flavonoid (C3) extracted from Glycyrrhiza glabra leaves. In fatty acid-overloaded HepG2 cells, C3 stimulated AMPK activation and significantly reduced lipid droplets in an AMPK-PKA dependent manner. Kinome profiling and proteomics revealed the activation of kinases associated with lipolysis, autophagy, and cellular stress responses pathways. Mechanistically, C3 enhanced lipolytic activity, induced autophagy, improved mitochondrial function, and stimulated β-oxidation. Furthermore, in vivo experiments using a Drosophila melanogaster model fed a high-fat diet showed that C3 administration reduced the number of lipid droplets in fat bodies and rescued locomotor performance. In summary, this natural compound protects against early MAFLD by triggering PKA/AMPK mediated lipid catabolism.

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From roots to roofs: Evaluating Nature-based Solutions integrating Ecosystem Services and life-cycle thinking

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SYSTEM DYNAMICS; LIFE CYCLE ASSESSMENT; INDUSTRIAL ECOLOGY; PHYTOREMEDIATION; URBAN REGENERATION

Nature-based Solutions (NbS) require integrated evaluation approaches to capture both their multifunctional benefits and their environmental impacts. This work combines ecosystem services (ES) assessment with Life Cycle Assessment (LCA) to evaluate NbS along their entire life cycle. The methodology has been tested on two case studies. The first concerns the regeneration of an urban square through an intensive green roof, where a biodiversity indicator was developed to widen the ES assessment. The second addresses the phytoremediation of hydrocarbon-contaminated soil using poplar trees, where a system-dynamics model was applied to simulate plant growth and the related ES. In both cases, ES were assessed alongside LCA-based impact indicators, allowing a comparison between provided benefits and induced environmental burdens. This combined approach contributes to a more robust framework for supporting decision-making in the design, implementation, and management of sustainable NbS.

* To attend these sessions, participants are required to sign a confidentiality agreement to ensure that all research presented remains protected and is not shared without authorization

s15.

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Fructooligosaccharide-driven probiotic metabolism reduces hepatocyte lipid accumulation in an in vitro human gut microbiota model

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PROBIOTICS, FOS, HUMAN GUT MICROBIOTA, IN VITRO MODEL, METABOLIC-ASSOCIATED-FATTY-LIVER-DISEASE

The human gut microbiota (HGM) plays a pivotal role in host metabolism through the production of bioactive metabolites from dietary compounds. This PhD project investigates how selected carbon sources shape microbial interactions and metabolic outputs using a defined in vitro HGM model. Fructooligosaccharides (FOS) were used to evaluate substrate-driven community dynamics, functional gene expression, and metabolite production. The resulting microbial metabolites were then assessed in a HepG2 steatosis model of metabolic dysfunction-associated fatty liver disease (MAFLD). FOS fermentation promoted the production of short-chain fatty acids and other fermentation products, which reduced lipid accumulation and cd36 expression, supporting a role for microbiota-derived metabolites in the modulation of hepatic lipid metabolism. Current work is expanding this approach to additional carbon sources to further investigate microbial interactions and metabolic functionality.

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Do strain diversity and/or dietary context determine the pathogenic potential of Collinsella aerofaciens in metabolic inflammation?

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COLLINSELLA AEROFACIENS, GUT MICROBIOTA, NON-COMMUNICABLE DISEASES, INTESTINAL PERMEABILITY, WESTERN DIET

Increasing evidence indicates that gut microbiota alterations contribute to the development of non-communicable diseases (NCDs). Among the taxa associated with these conditions, Collinsella aerofaciens has been proposed as a context-dependent pathobiont contributing to intestinal permeability, low-grade inflammation and gut-liver axis dysfunction1. We hypothesize that its pathogenic potential depends on both dietary context and strain-level diversity. To investigate this, we first assessed the type strain DSM 3979^T in a Caco-2 NF-κB reporter model, where it induced significant NF-κB activation. We then evaluated its growth in ex vivo fecal batch cultures inoculated with fecal samples collected from healthy volunteers following balanced, high-fat/low-fiber or Western diets. Dietary background markedly influenced bacterial fitness, supporting a role for diet in promoting C. aerofaciens expansion. Ongoing studies are extending these findings to multiple strains and an in vivo mouse model.

1- Gargari et al. Collinsella aerofaciens as a predictive marker of response to probiotic treatment in non-constipated irritable bowel syndrome. Gut microbes vol. 16,1 (2024): 2298246. doi:10.1080/19490976.2023.2298246

S17.

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Stn1 supports Mec1 function in protecting stalled replication forks from degradation

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YEAST, GENOME STABILITY, DNA DAMAGE, REPLICATION STRESS, CST COMPLEX

Replication stress threatens genome stability by exposing stalled replication forks to nucleolytic degradation and excessive single-stranded DNA accumulation (ssDNA). Although the checkpoint kinases Mec1 and Rad53 protect stalled forks, the mechanisms limiting aberrant DNA processing remain unclear. We identify the CST subunit Stn1 as a key factor cooperating with Mec1 to preserve replication fork integrity under replication stress. A gain-of-function Stn1 allele suppresses the hypersensitivity of Mec1-deficient cells and reduces ssDNA accumulation at stalled forks, whereas Stn1 loss of function exacerbates fork degradation. Mechanistically, Stn1 counteracts Mre11-, Exo1- and Sgs1- mediated resection by promoting Polα–primase-dependent fill-in synthesis and, predominantly, by restricting nuclease association with stalled forks. Stn1 also limits nuclease recruitment at DNA double-strand breaks, revealing a broader role in regulating DNA end processing and maintaining genome stability.

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Microbial dynamics between people and the built environment

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MICROBIOME, HOSPITAL, SKIN, ENVIRONMENT, HUMAN HEALTH

Hospitals are dynamic microbial ecosystems shaped by sanitation, patient turnover, and human activity. We investigated hospital microbiome development over time and microbial exchange between patients and the clinical environment. Two campaigns were conducted at San Gerardo Hospital (Monza, Italy). A one-year longitudinal study monitored three newly opened wards, while a second study assessed short hospital stays through environmental sampling before admission and skin sampling from patients' dominant hands before and after visits.Overall, 1,300 environmental and 260 skin samples were analyzed by 16S rRNA gene V3–V4 sequencing. Diversity, differential abundance, core microbiome, source–sink, and microbial overlap were assessed.
Hospital surfaces were dominated by skin-associated genera, including Staphylococcus, Corynebacterium, Cutibacterium, and Finegoldia. Short-term exposure promoted bidirectional microbial exchange, highlighting hospitals as dynamic ecosystems and supporting the importance of understanding microbial transfer for infection prevention.

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The Gut Microbiota as a Biological Interface Between Dietary Interventions and Host Health

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GUT MICROBIOTA, DIET, NUTRACEUTICAL, PROBIOTIC, PREBIOTIC

Nutraceuticals and dietary components are external factors influencing host health via gut microbiota-mediated mechanisms[1]. Within this framework, the microbiota responds to dietary and functional stimuli that reshape its composition and metabolic activity, resulting in beneficial or detrimental host effects. Three complementary approaches explored this concept, each focused on a distinct dietary intervention: sucralose, an artificial sweetener whose microbial biotransformation has recently been linked to dysbiosis[2]; fungal enzyme blends, designed to enhance nutrient bioaccessibility and modulate downstream microbial metabolism[3]; and botanical extracts and microbial exopolysaccharides (EPS), evaluated as potential prebiotics selectively promoting beneficial gut bacteria[4]. Across all three studies, the gut microbiota emerges as the key mediator linking dietary interventions to host health, acting as the biological interface translating nutritional stimuli into physiological outcomes.

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2- Morder, K. M., Nguyen, M., Wilfahrt, D. N., Dahmani, Z. L., Burr, A. B. P., Xie, B., Morikone, M., Nieves-Rosado, H., Gunn, W. G., Hurd, D. E., Wang, H., Mullett, S. J., Bossong, K., Gelhaus, S. L., Rajasundaram, D., Kane, L. P., Delgoffe, G. M., Das, J., Davar, D., & Overacre-Delgoffe, A. E. (2025). Sucralose Consumption Ablates Cancer Immunotherapy Response through Microbiome Disruption. Cancer discovery, 15(11), 2278–2297. https://doi.org/10.1158/2159-8290.CD-25-0247
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4- Razzak, M. A., Kim, H., Haque, M. A., Jang, M. J., Song, S., Talari, A., Chittepu, L. D., & Ku, S. (2026). The Prebiotic and Techno-Functional Potential of Microbial Exopolysaccharides for Human Health and Food Systems. Comprehensive reviews in food science and food safety, 25(2), e70406. https://doi.org/10.1111/1541-4337.70406

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Effects of Combined Istaroxime and Levosimendan Treatment on Ca2+ Handling and Contractility in Mouse Cardiac Preparations

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CA2+ SENSITIZERS, HF, CA2+ HANDLING, CONTRACTILITY

Direct myofilament stimulation may improve systolic function but impair relaxation. Combining the SERCA2a activator istaroxime (ISTA) with the Ca2+ sensitizer levosimendan (LEVO) could overcome this limitation.
We evaluated the effects of ISTA+LEVO on Ca2+ handling and contractility in murine cardiac preparations. Ca2+ dynamics were assessed in isolated ventricular cardiomyocytes and contractility in multicellular preparations. Drugs were tested alone and in combination, with additional experiments using the PDE3 inhibitor cilostamide (CILO). ISTA+LEVO accelerated Ca2+ transient decay and reduced diastolic Ca2+. ISTA enhanced SR Ca2+ uptake and twitch amplitude. LEVO unexpectedly accelerated Ca2+ decay without increasing contractility; this effect disappeared with CILO, indicating PDE3/PKA involvement. Although ISTA+LEVO improves Ca2+ handling, the lack of LEVO-induced inotropy limits assessment of its therapeutic potential. Preliminary human data suggest species-specific differences.

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Synthetic biology applied to the biomanufacturing of plant natural products of pharmaceutical interest

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SACCHAROMYCES CEREVISIAE, SYNTHETIC BIOLOGY, METABOLIC ENGINEERING, PLANT NATURAL PRODUCTS

Plants are a major source of pharmaceutically relevant secondary metabolites, but their production through plant extraction or chemical synthesis often raises sustainability concerns. In this project, different approaches were applied to develop microbial and/or enzymatic platforms for the production of biosynthetic intermediates that serve as precursors to plant-derived bioactive molecules. Recombinant Saccharomyces cerevisiae strains were engineered to convert simple and readily available amino acids into target compounds. In addition, enzyme and protein engineering strategies were employed to improve catalytic performance. Enhanced production of valuable intermediates was achieved by combining heterologous enzyme expression, metabolic pathway optimization and process development. The results obtained will be presented, highlighting the production of those intermediates and discussing future strategies aimed at further enhancing metabolite titers, yields, and productivity.

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Exploiting yeast surface display for whole cell biocatalysis in *Komagataella phaffii*

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KOMAGATAELLA PHAFFII, WHOLE-CELL BIOCATALYSIS, YEAST SURFACE DISPLAY, ENZYME IMMOBILIZATION, INDUSTRIAL BIOTECHNOLOGY

Recombinant enzymes are usually secreted and purified at the end of fermentation, but this can be costly. Whole cell biocatalysis (WCB) can reduce the number of steps required. Whole cells can also be easily removed from the reaction mixture, facilitating recycling in industrial settings. The cell membrane can slow down substrate and product exchange. Using yeast surface display, the enzyme is attached to the outer cell wall, overcoming membrane permeability limitations and possibly increasing enzymatic stability. In this work, we immobilized an inulinase from Kluyveromyces marxianus on Komagataella phaffii using a native GPI anchor. Its activity and stability were compared with the secreted enzyme. The ratio of cell-associated enzymatic activity to that detected in the supernatant was higher in the presence of the anchor, suggesting that immobilization was successful. A bacterial cohesin–dockerin system was also tested to try to enhance the catalytic activity associated with each cell

s23.

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Safety assessment of perovskite nanoparticles within a Safe and Sustainable by Design approach

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PEROVSKITE NANOPARTICLES, SAFE AND SUSTAINABLE BY DESIGN, IN VITRO TOXICITY, HUMAN HAZARD ASSESSMENT

The European Green Deal promotes innovative, sustainable, and safe materials. In this context, the INTEGRANO project assesses nanomaterial safety and sustainability within the Safe and Sustainable by Design (SSbD) framework. This study focuses on strontium-iron-cerium perovskite nanoparticles doped with bio-silica, designed for catalytic membranes in wastewater treatment. The materials were produced by varying key synthesis parameters through a Design of Experiments (DoE) approach, then characterized and tested in vitro. Human A549 lung epithelial cells were exposed to different formulations to assess cell viability, pro-inflammatory response, oxidative stress, and DNA damage. Results showed material-dependent responses. Further experiments evaluated the potential ROS-scavenging behavior of the perovskite formulations. Future work will extend the evaluation to complex lung models, including A549, THP-1, and MRC-5 co-cultures, to investigate inflammatory and pro-fibrotic mechanisms.

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Enhanced prediction of drug-induced gastrointestinal toxicity in a human gut-on-chip

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GUT-ON-CHIP, MIVO, DGIT, TOXICITY MODEL

Drug-induced gastrointestinal toxicities (DGIT) cause patient non-compliance and treatment delays, yet existing models poorly replicate human physiology. This study utilises the MIVO® gut-on-chip platform to implement fluid-flow-induced shear stress, accelerating Caco-2:HT-29-MTX cell maturation and barrier function to 7 days (versus 21 days statically) [1]. Eight reference drugs were evaluated to assess DGIT via barrier integrity (TEER, permeability), cell viability (MTT), and morphology (ZO-1/AQP3). Idarubicin, afatinib, and cisplatin induced overt epithelial toxicity. Docetaxel caused selective barrier leakage and focal architectural disruption without acute cytotoxicity. Metformin served as a true negative. Tacrolimus, sorafenib, and 5-FU acted as false negatives, mapping the model's scope by highlighting the requirement for immune, endothelial, or crypt compartments. This platform offers a predictive, animal-free tool for drug testing.

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s25.

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Unraveling the Potential of L-Ido-Configured Glycomimetics as Versatile Glycosidase Modulators

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L-IDO GLYCOMIMETICS, IMINOSUGARS, CYCLITOLS, IDUA, GBA2

We describe the development of L-ido-configured glycomimetics, from iminosugar analogues of L-idose and L-iduronic acid to cyclitol-based scaffolds for glycosidase modulation. A versatile synthetic approach provided a library of 1-deoxy-L-idonojirimycin derivatives, whose conformational properties were studied by computational and NMR methods.[1,2] Selected compounds acted as active-site binders of α-L-iduronidase (IDUA) and provided a proof of concept for enzyme activity enhancement in cell-based assays. Beyond IDUA modulation, inhibition studies and literature data revealed higher potency toward β-glucosidase 2 (GBA2) than β-glucocerebrosidase (GCase), prompting the design of L-ido-configured aziridines as selective GBA2 inhibitors and probes.[3] Overall, L-ido glycomimetics emerge as versatile tools for glycosidase modulation, spanning from pharmacological chaperones to covalent enzyme inhibitors.

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2- Artola M. et al., Chemistry - A European Journal 2018, 24.
3- Ghisaidoobe A.T. et al., Journal of Medicinal Chemistry 2014, 57, 9096–9104.

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Posters

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Creating pollinator-friendly habitat through an interactive decision-support app

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POLLINATORS, PLANTS, ECOLOGY, HABITAT RESTORATION

We show the first demo of a shiny app suggesting the right plants to attract local pollinators. By integrating the European Atlas of Plant-Pollinator Associations (EUROAPPA) with plants and pollinator traits, users can select their pollinator of interest and receive suggestion tailored to their local land conditions.

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Towards a Dynamic Blood-Brain Barrier-on-Chip Model for Studying Tumor Cell Interaction and Barrier Maturation

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BLOOD-BRAIN BARRIER; ORGAN-ON-CHIP; DYNAMIC CULTURE; ENDOTHELIAL BARRIER; TUMOR CELL INTERACTION

Dynamic organ-on-chip models offer a promising strategy to reproduce blood-brain barrier (BBB) physiology and investigate tumor cell interactions with brain-like vascular interfaces. Within the Mac4Me project, a dynamic BBB module is being developed for integration into a multicompartmental platform linking circulating cells with brain and liver target tissues. Preliminary work established endothelial monolayers on porous inserts under static and MIVO® dynamic conditions, assessing barrier performance by TEER, FITC-dextran permeability, and immunofluorescence of endothelial organization and junctional markers. GFP-positive cancer cells were then perfused under flow to evaluate adhesion and potential trans-endothelial migration. The next phase will incorporate brain vascular pericytes and astrocytes within a collagen hydrogel opposite the endothelial layer, aiming to promote barrier maturation and generate a physiologically relevant BBB-on-chip model for cancer trafficking studies..

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Development and optimization of functional nanomaterials for physical modulation of cell aging processes

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LIGHT, POLYMER NANOPARTICLES, ENDOTHELIAL CELLS, SENESCENCE, NITRIC OXIDE

Nitric Oxide (NO) is a key regulator of cellular aging and represents a promising therapeutic target. Many studies highlighted its pivotal role in skin homeostasis and pathology(1). Although several biotechnology strategies have recently been reported to modulate NO, most fail to meet the necessary requirements or precise control (i.e., high spatio-temporal resolution, reliability, reversibility) and non-invasiveness(2).
This study introduces light-sensitive conjugated polymer nanoparticles (NPs), as a new strategy to optically modulate NO-pathways and to regulate skin homeostasis and aging processes, across several cell models.
We demonstrate NPs capability to dynamically switch between high and low NO-levels, to modulate barrier integrity, and to regulate cell metabolism and senescence.
Future studies will focus on evaluating these stimuli-responsive NPs in advanced 3D skin models and in vitro disease environments, while further elucidating the mechanisms underlying NO modulation.

1- Kim JH et al. Biomol Ther. 2023 Jul 1;31(4):388-394. doi: 10.4062/biomolther.2023
2- Andrabi SM et al. Adv Sci. 2026 Apr;13(23):e21942. doi: 10.1002/advs.202521942.

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Pollinator decline in a changing world: characterizing the pollination ecosystem services and the solutions for habitat enhancement

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POLLINATORS, ECOSYSTEM SERVICES, ECOLOGICAL RESTORATION, HABITAT MANAGEMENT

Biodiversity underpins essential ecosystem services, with pollination playing a key role in maintaining plant diversity and food production. However, pollinator declines highlight the need for ecological restoration and habitat management. To address this challenge, the Lombardy Living Lab was established within the Horizon EU projects Butterfly and ProPollSoil, connecting green areas, farms, community gardens and stakeholders across Milan.
Surveys in 3 orchard crops provided a baseline assessment of pollinator and flowering plant diversity and their contribution to ecosystem services and crops. The analysis of the cherry supply chain confirmed its strong dependence on insect pollination. Habitat enhancement measures (reforestation and flower strips) were evaluated, showing positive effects on flower-visiting and ground-nesting pollinators. These findings support the development of targeted conservation actions to promote pollinator diversity and sustainable food production. .

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A novel role for Sox2 in differentiated thalamic neurons: defining thalamic identity and visual system connectivity

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SOX2, VISUAL SYSTEM, THALAMUS, MOUSE

Mutations in the gene encoding the transcription factor SOX2 cause neurodevelopmental visual disorders. SOX2 not only is required for neural stem cells self-renewal, but also for the differentiation of neurons of the thalamic dorsolateral geniculate nucleus (dLGN), which connects the eyes with the visual cortex. Conditional knockout of Sox2 in the mouse thalamus impairs dLGN development and visual circuit formation. RNA-seq of neonatal Sox2 mutant dLGN revealed that SOX2 regulates genes involved in axon guidance and synaptogenesis. To elucidate the phenotype due to SOX2 loss we are studying its targets both in vivo and in vitro in primary thalamic neuronal cultures. We are assessing defects in visual circuit formation through neuronal tracing experiments. Finally, we are identifying cell types sensitive to SOX2 loss through spatial transcriptomics studies with VISIUM HD. Overall, this work aims to define the Sox2-dependent network underlying thalamic identity and visual connectivity.

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Exploring Mitochondrial Metabolic Specialization through Computational Modeling

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MITOCHONDRIAL METABOLISM; CONSTRAINT-BASED MODELING; METABOLIC SPECIALIZATION

Mitochondria play a central role in cellular metabolism, energy production, and biosynthesis, and their functional heterogeneity is increasingly recognized as a determinant of cellular phenotypes. Computational metabolic models provide a quantitative framework to investigate how mitochondrial metabolic organization shapes intracellular metabolism. This project develops constraint-based metabolic models incorporating thermodynamic and enzyme constraints to refine feasible metabolic flux distributions and improve the biological consistency of model predictions. Models including multiple mitochondrial compartments are used to investigate the emergence of metabolic specialization and its impact on intracellular flux organization, supporting the generation of experimentally testable hypotheses. A complementary component explores the integration of metabolism and cellular growth through coarse-grained models to investigate growth dynamics, resource allocation, and biomass production.

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Molecular Dynamics Investigation for O2 Diffusion Mechanism in the Protective CbA5H Hydrogenase

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[FEFE]-HYDRIGENASE, MOLECULAR DYNAMICS, O2-RESISTANCE, H2-PRODUCTION

[FeFe]-hydrogenases are efficient biocatalysts for H2 conversion but are generally highly sensitive to O2. The Clostridium beijerinckii [FeFe]-hydrogenase (CbA5H) exhibits a unique O2 protection mechanism in which a conformational change enables a conserved cysteine (C367) to bind the distal Fe of the H-cluster. However, how O2 reaches the active site and triggers Hinact formation remains unclear. Here, we combine unbiased molecular dynamics (MD) and Random Accelerated Molecular Dynamics (RAMD) simulations to investigate O2 diffusion in CbA5H. We identify three potential O2 pathways, characterizing their length, radial profile, and bottlenecks, and highlighting key residues controlling diffusion. Comparison with other [FeFe]-hydrogenases, including Clostridium pasteurianum I (PDB: 6N59), provides structural insight into the CbA5H protection mechanism and supports future engineering of O2-tolerant biocatalysts for sustainable H2 production.

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hiPSCs-derived cardiomyocytes treated with Angiotensin II to recapitulate heart failure in vitro

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HIPSC-CMS, HEART FAILURE, ANGIOTENSIN II

Heart Failure (HF) is a complex syndrome characterized by impaired cardiac function resulting from molecular, structural, and functional abnormalities, with a continuously rising prevalence. Despite several in vivo models have been used for the study of HF, an efficient in vitro platform is still lacking. Starting from this, our project aims to fill the gap generating an in vitro model that recapitulates HF phenotype exploiting human induced pluripotent stem cells derived cardiomyocytes (hiPSC-CMs). Specifically, the HF-induction is guided by the cell treatment with Angiotensin II (AngII, 100nM), an established molecule known to trigger cardiac remodelling in in vivo models. Our project aims to characterize time-dependent effects of AngII in hiPSC-CMs at the molecular, metabolic and functional level. The achievement of an established and accepted cardiac cell platform with a failing phenotype would be relevant for preclinical in vitro drug testing directly in human CMs.

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Exploring the role of histone H3 methylation in response to DNA double strand breaks

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SACCHAROMYCES CEREVISIAE, HISTONE METHYLATION, DNA DOUBLE STRAND BREAKS, GENOME STABILITY, DNA REPAIR

Genome stability relies on efficient DNA repair. DNA double-strand breaks (DSBs) are the most cytotoxic lesions and, if improperly repaired, can lead to genome instability and cancer. DNA repair occurs within chromatin, where histone post-translational modifications (PTMs) regulate chromatin structure and the recruitment of repair factors. Although several PTMs contribute to the DNA damage response, the role of histone methylation remains incompletely understood.

Using Saccharomyces cerevisiae, we investigate the role of histone H3 methylation in DSBs repair. We identified genetic interactions between histone methyltransferases/demethylases, and DSB repair genes, suggesting a functional role for histone methylation in this process. Moreover, we are analysing the effects of methylases and demethylases inactivation on the cellular response to DSBs. In parallel, we are using a ChIP-seq approach to monitor changes in histone methylation following the induction of a site-specific DSB.

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Identification of natural antiaggregant bioactive compounds in Lamiaceae family: an interdisciplinary approach to target protein-misfolding diseases

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BIOPROSPECTING, MEDICINAL PLANTS, BIOACTIVE COMPOUNDS, PARKINSON'S DISEASE, PROTEIN AGGREGAGTION

The One Health idea recognizes the deep interconnection between human, animal and environmental health. According to this, the bioprospecting approach looks for bioactive molecules in biodiversity as a potential strategy to prevent/treat human diseases. By using an innovative evolutionary based tool to investigate medicinal products in plants, we have identified 111 species belonging to the Lamiaceae family (from 2348 taxa), that have high probability to have neuroprotective properties against Parkinson's Disease (PD). A representative set of species from the *in silico* screening was sampled, leave extracts were prepared using ultrasound-assisted extraction (UAE), and then tested on a neuronal model of PD to investigate their antiaggregant properties. The integration of bioactivity evaluation on cell cultures and chemical profiling will enable the identification of the most promising extracts for the isolation of bioactive compounds and the investigation of their mechanisms of action.

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Keynote Speakers

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Perceptual Reality and Scientific Epistemology: An Evolutionary Perspective on Cognitive Biases, Misconceptions, and the "Fitness" Contribution of Scientific Knowledge

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How does an organism evolved for reproductive fitness navigate objective reality? This seminar explores the profound tension between biological survival and the pursuit of objective truth. First, we will examine the divergence between adaptive value and truth-value in perceptual and cognitive systems, using cognitive biases and optical illusions as case studies of evolved information processing. Then, we will discuss the epistemological role of the scientific method as a corrective to naïve realism, addressing common misconceptions in the public understanding of evolutionary theory. Finally, we will address the apparent paradox of why scientific frameworks often face widespread public rejection and suspicion despite our species' total reliance on their technological outputs, examining how cognitive constraints, in-group/out-group dynamics, and naturalistic fallacies shape the persistence of scientific misinformation.

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Life After the PhD: There Is No Standard Protocol.

How curiosity, adaptability, and a few wrong turns shaped my career path.

Lorenzo Signori
PhD in Industrial Biotechnology and over 10 years of experience in the pharmaceutical industry. Background spans from external manufacturing, CDMO management, supply chain, and project management.

CAREER PLANNING, SELF-AWARENESS, CONTINUOUS LEARNING, DECISION-MAKING, PROFESSIONAL GROWTH

Many of us begin our careers believing that a clear plan, technical expertise, and hard work will determine where we end up. Reality is often more complex. This talk reflects on a professional journey shaped not only by planning, but also by opportunities, unexpected events, changing priorities, successes, and mistakes. Drawing on experiences industrial biotechnology, project management, supply chain, external manufacturing, and leadership roles, I will share lessons learned while navigating an evolving professional landscape. The key message is that there is no standard protocol for building a career. While external factors continuously reshape our options, we can actively define and refine our own career model through self-awareness, goal setting, and adaptability. Ultimately, career growth begins with understanding who we are, what motivates us, and how our priorities evolve over time.

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Cose dette Mare va in Montagna

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Graziella Pupillo, Department of Earth and Environmental Sciences, University of Milano-Bicocca, Milan, Italy; Marine Research and Higher Education (MaRHE) Center, University of Milano-Bicocca, Magoodhoo, Faafu Atoll, Maldives.

Cose dette Mare is a science communication and Ocean Literacy project. At its core is an independently produced podcast that explores the ocean as a complex, interconnected system that is present in every aspect of our daily lives—from science and the environment to history, literature, art, and culture.

PODCAST; SCIENCE COMMUNICATION; ENVIRONMENT; MARINE SCIENCES; OCEAN LITERACY

Cose means "things", a word that can refer both to something we know well and to something vague, or that we cannot name. The ocean is much the same: we know only a fraction of it, while much remains unknown and even unimaginable. This is where our work begins. We talk about the ocean “come se fossimo in un caffè” (“as if we were sitting in a café”): with simple, engaging language grounded in science but avoiding technical terms, enriched by references to history, literature, pop culture, and everyday life. During this talk, we will explore how this approach can move conversations about the ocean beyond academia and into everyday spaces, while reimagining scientists not only as highly trained professionals, but also as open, interdisciplinary individuals aware of the limits of their own knowledge and willing to engage not only with what can already be measured and observed, but also with what can still be imagined.

18th PhD meeting TECSBI 2026