17th PhD meeting

TECSBI

2025

BOOK OF ABSTRACTS

22-24 SETTEMBRE

UNIVERSITY OF MILANO-BICOCCA

VILLA CAGNOLA - Via Cagnola, 17/19 - 21045 GAZZADA SCHIANNO (VA)

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

BtBs Department of Biotechnology and Biosciences

SCUOLA DI DOTTORATO BICOCCA

TeCSBi PhD TECNOLOGIE CONVERGENTI PER I SISTEMI BIOMOLECOLARI

SPONSORED BY:

Converging Technologies for Biomolecular Systems (TeCSBI)

17th PhD Meeting - 22/24 September 2025
UNIVERSITY OF MILANO-BICOCCA

PROGRAM

Monday 22

14.00-14.10 Opening Day 1

14.10-14.30 **s1. Mirko Frigerio Verga** *

Overcoming enzyme production instability in Escherichia coli for application in the agropharmaceutical field

14.30-14.50 **s2. Marco Barreca**

Longitudinal Clustering of TNBC patients using transcriptomics data: a trajectory distance-based approach

14.50-15.10 **s3. Elisa Toini**

Phylogenetic approach reveals plants with high medicinal potential

10.10-10.30 **s4. Tommaso Sassi** *

Development of an Escherichia coli cell-factory for the industrial production of 5-methylpyrazine-2-carboxylic acid

15.30-16.30 Poster Session 1

16.30-17.30 **ADI**
Meeting with the PhD students

Tuesday 23

8.50-9.00 Opening Day 2

9.00-9.20 **s5. Angela Maria Giada Giovenale**

Neurogenesis in Smith-Magenis Syndrome: When Brain Development Go Awry

9.20-9.50 **s6. Giulia Ghisleni**

A Participatory and Evolutionary Approach to Urban Microbiome Research: Reuniting Microbiology and Society

9.50-10.10 **s7. Martina Dramis** *

Optimizing culture conditions for biomanufacturing bacterial cellulose and tailoring its functionalization

10.10-10.30 **s8. Lorenzo Taglietti**

L-Iduronic Acid-Type 1-N-Iminosugars as Pharmacological Chaperones for the Rescue of α-L-Iduronidase in Mucopolysaccharidosis Type I

10.30-11.30 Coffee Break +
Poster Session 2

11.30-11.50 **s9. Miriam Kuku Afanga** * 🌐

Identification of miRNA-based biomarkers predictive of lung cancer treatment response, and mechanisms involved in lung cancer progression.

11.50-12.10 **s10. Francesca Misitano** * 🌐

Modulation of Ca2+ handling by combined administration of Istaroxime and Levosimendan in mouse ventricular cardiomyocytes

12.10-12.30 **s11. Stefano Bianchini**

Anticancer properties of plant extracts on colorectal cancer cell lines

12.30-12.50 **s12. Alessia Metallo**

Istaroxime Prevents AngiotensinII-Induced Remodeling in Pulmonary Artery Smooth Muscle Cells

12.50-14.10 Lunch Break

14.10-15.00 **is1. Francesco Moccia**
UNIMOL

A journey through intracellular Ca2+ signaling: understanding physiology to interfere with pathology

15.00-15.20 **s13. Alice Armanni** 🌐

The built environment and microbiome in human health - insights from everyday life and the hospital environment

15.20-15.40 **s14. Alice Italia** *

Functional impact of Toll-like Receptor 4 (TLR4) modulation in lung fibrosis-associated fibroblasts

15.40-16.00 **s15. Gergo Borka**

Evaluating Chemotherapeutic Drug Induced Gastro-intestinal Toxicity (DGIT) using a multi-compartimental Gut-on- Chip Model

16.00-16.30 Coffee Break

16.30-16.50 **s16. Chiara Florindi**

"Amphiphilic membrane-targeted phototransducers for non-genetic optical stimulation of carciac bioelectricity"

16.50-17.10 **s17. Edvige Vulcano**

Interrogating Amyotrophic Lateral Sclerosis Signatures in TDP-43 G376D human induced Neural Stem Cells

17.10-17.30 **s18. Rosa Ranalli**

Cities for pollinators: supporting biodiversity through urban habitats

17.30-17.50 **s19. Laura Beretta** *

Early Insights, Lasting Impact: Mechanistic Enzymology for Characterizing Hit Compound Mechanisms of Action

Wednesday 24

8.50-9.00 Opening Day 3

9.00-9.20 **s20. Serena Seminara**
Investigating the involvement of the Wiskott-Aldrich Syndrome Protein (WASp) in the function of brain-resident immune cells

9.20-9.50 **s21. Maria Chiara Barbera**
Hijacking the clock: Epigenetic age rewiring via miR-29 modulation

9.50-10.10 **s22. Alessia Lambiase**
Neuroprotective effects of plant bioactive compounds on eukaryotic models of Parkinson's disease

10.10-10.30 **s23. Susanna Perotti**
Exploring the Microbial Biodiversity of Kombucha for Novel Probiotic and Postbiotic Candidates

10.30-11.30 Coffee Break + Poster Session 3

11.30-11.50 **s24. Giorgia Ruotolo**
Modeling Primary Cilium Defects in Joubert Syndrome using iPSC-Derived Neural Stem Cells

11.50-12.10 **s25. Barbara Zerbato**
PGM3 Inhibition as a Novel Strategy to Induce BRCAness in HR-Proficient Pancreatic Cancer Cells

12.10-12.30 **s26. Francesco Abbiati**
Bioactive compounds and healthy aging: search for new nutraceutical compounds through the experimental model of chronological lifespan in yeast

12.30-12.50 **s27. Beatrice Colombo**
Wild bees adaptation to urbanization: a multi-Omic approach to implement innovative conservation and ecological transition strategies

12.50-14.10 Lunch Break

14.10-15.00 **is2. Luca De Gioia**
UNIMIB
"Life Is good" and other misconceptions. Breve itinerario tra i luoghi comuni e sorprendenti scoperti

15.00-15.20 **s28. Maria Rita Chelazzi**
Investigating the role of the SOWAHC-DIAPH1 complex in physiology and cancer

15.20-15.40 **s29. Luca Moretti**
Natural products targeting Amyloid-β aggregation: spectroscopic and biophysical approaches for Alzheimer's disease prevention

15.40-16.00 **s30. Maddalena Bracchi**
Design and 3D fabrication of functional meniscal scaffolds

16.00-16.30 Coffee Break

16.30-16.50 **s31. Francesco Lapi** 🌐
Multi-omics data analysis to characterize sex-specific metabolic shifts during embryo development

16.50-17.10 **s32. Lidia Favaretto**
The evaluation of Nature-based Solutions through a life-cycle thinking approach: key challenges and opportunities

17.10-17.30 **s33. Flavio Corallo** *
Stn1 supports Mec1 function in protecting stalled replication forks from degradation

COLOR CODE

Industrial Biotech **Health and Biodiversity** **Biomedical and Health**

* 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

🌐 Online presentation

POSTER SESSIONS

Mon 22, 15.30-16.30 Poster Session 1

p1. Andrea Banfi
Harnessing Mirror-Image Peptides: Nanoparticle Vectors for Nucleic Acid Delivery in Cancer Treatment

p2. Beatrice Pizzelli
The role of Collinsella aerofaciens in Non-Communicable Diseases: potential implication in pathogenesis through gut-liver axis activation

p3. Fabio Angelini
Lactic Acid Bacteria, Aromatic Amino Acids and Human Health: Two Functional Approaches

p4. Francesca Vincenti
Resolving HSC heterogeneity with integrated single-cell Multi-Omics

Tue 23, 10.30-11.30 Poster Session 2

p5. Francesco Bellusci *
Synthetic biology applied to the biomanufacturing of plant natural products of pharmaceutical interest

p6. Hind Moukham *
Glabranin as a natural modulator of AMPK signaling and lipid metabolism in NAFLD

p7. Linda Molteni
Better Together: NMR Spectroscopy and Other Biophysical Tools for the Comprehensive Characterization of Prenylflavonoids Anti-Amyloidogenic Properties

p8. Margherita Finazzi
Design and characterization of an in vitro reconstructed human gut microbiota to model microbe-microbe and host-microbe reciprocal interactions

Wed 24, 10.30-11.30 Poster Session 3

p10. Radhika Dhekane
Multi-factor fluid-dynamic model of the tumor microenvironment

p11. Stefano Cervellera
Multidimensional Integrated Quantitative Approach To Assess Safety And Sustainability Of Nanomaterials In Real Case Life Cycle Scenarios Using Nanospecific Impact Categories

p12. Stefano Cozzi
Expanding progenitor-like cells via CN-NFAT inhibition to uncover additional differentiation mechanisms

Speakers

s1. Industrial Biotech

Mirko Frigerio Verga
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Overcoming enzyme production instability in Escherichia coli for application in the agropharmaceutical field

Mirko Frigerio Verga[1], Daniela Bucchieri[1], Beatrice Serati[1], Valeria Mapelli[1], Immacolata Serra[1], Giovanni Pozzi[2], Marco Nicolini[2]

[1] University of Milano-Bicocca
[2] Sipcam Oxon

AGROPHARMACEUTICALS, ENZYMES, ANTIBIOTIC, SCALE-UP, ESCHERICHIA COLI

Sipcam Oxon, the company co-financing this PhD project, produces agropharmaceuticals via chemical synthesis. Chiral molecules play a critical role in this field, their activity depending on a specific stereoisomer, making traditional synthesis inefficient. As a result, enzymatic approaches are increasingly utilized. In this work, E. coli is the host for recombinant enzyme production, with plasmid maintenance relying on antibiotic resistance. The current process, based on a beta-lactam antibiotic has low stability, limiting scalability.
To address this, we optimized both fermentation conditions and culture media, successfully transferring a more robust process to pilot scale. In parallel, a new E. coli production strain carrying a more stable antibiotic resistance cassette was built and tested, demonstrating improved performance and plasmid retention. Future efforts will focus on refining downstream processing and implementing whole cell biocatalysis for enhanced synthetic performance.

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Marco Barreca
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Longitudinal Clustering of TNBC patients using transcriptomics data: a trajectory distance-based approach

Marco Barreca[1 2], Oscar Rueda[3], Maurizio Callari[2], Daniela Besozzi[4 5]

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[2] Fondazione Michelangelo
[3] MRC, Biostatistics Unit, University of Cambridge
[4] Department of Informatics, Systems and Communication, University of Milano-Bicocca
[5] Bicocca Bioinformatics, Biostatistics and Bioimaging (B4) Research Centre

BREAST CANCER, TNBC, TRANSCRIPTOMICS, BIOINFORMATICS, LONGITUDINAL ANALYSIS

Triple-negative breast cancer (TNBC) is an aggressive and heterogeneous subtype with limited treatment options. The modulation of gene expression during treatment may provide valuable insights into response and resistance onset1, but current methods aren't developed to capture such longitudinal transcriptomic patterns.
We developed a strategy designed to cluster TNBC patients based on gene expression dynamics across multiple timepoints (baseline, Day 1 Cycle 2, and surgery). We selected the most variable signatures over time and evaluated trajectory distance-based metrics to group patients by expression patterns, considering both magnitude and direction of change. Our approach was benchmarked against established methods as functional data analysis (FDA)2,3 and latent class analysis (LCA)4, to compare clustering performance. This unsupervised analysis revealed clinically relevant patient subgroups, underlying the impact of integrated signatures dynamics on tumour progression prediction.

1. Park, Y. H., Lal, S., Lee, J. E., Choi, Y. L., Wen, J., Ram, S., ... & Kan, Z. (2020). Chemotherapy induces dynamic immune responses in breast cancers that impact treatment outcome. Nature Communications, 11(1), 6175.
2. Schmutz, A., Jacques, J., Bouveyron, C., Cheze, L., & Martin, P. (2020). Clustering multivariate functional data in group-specific functional subspaces. Computational Statistics, 35(3), 1101-1131.
3. Conde, S., Tavakoli, S., & Ezer, D. (2024). Functional regression clustering with multiple functional gene expressions. PloS one, 19(11), e0310991.
4. Fraley, C., & Raftery, A. (2007). Model-based methods of classification: using the mclust software in chemometrics. Journal of Statistical Software, 18, 1-13.

s3. Health and Biodiversity

Elisa Toini
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Phylogenetic approach reveals plants with high medicinal potential

Elisa Toini[1 2], Zecca Giovanni[1 2], Labra Massimo[1 2], Grassi Fabrizio[1 2]

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[2] NBFC, National Biodiversity Future Center, Palermo, Italy

MEDICINAL PLANTS, BIOPROSPECTING, BIOMOLECULES, PHYLOGENETIC METHODS, PREDICTION

Discovering beneficial molecules in plants is complex and requires significant time and resources. To streamline this process, a strategic approach is needed to identify species with high potential. A promising strategy involves phylogenetics, as closely related plant species tend to share biochemistry. This study proposes and applies a pipeline of phylogenetic methods to identify plants most likely to contain useful molecules. We combined monophyletic trees from the literature with medicinal plant data linked to disease, biological activity, or ethnobotanical use, sourced from databases or literature. All the data and subtrees were subjected to a series of phylogenetic methods. The results identified the "hot nodes", nodes related to the plants with the most potential and the descending subtrees were plotted. This study supports the efficacy of phylogenetic approaches in prioritizing plants for medicinal research.

Tommaso Sassi
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Development of an Escherichia coli cell-factory for the industrial production of 5-methylpyrazine-2-carboxylic acid

Tommaso Sassi[1], Luca Giuseppe Brambilla[1], Gabriele Rebuzzini[2], Marco Vanoni[1],

[1] University of Milano-Bicocca
[2] AMSA SpA

INDUSTRIAL MICROBIOLOGY, BIOMANUFACTURING, E. COLI, METABOLIC ENGINEERING, 5-METHYLPYRAZINE-2-CARBOXYLIC ACID

On 25 November 2020, the European Union adopted the Pharmaceutical Strategy for Europe. This initiative emphasize how the delocalization of basic and fine chemicals manufacturing outside the European Union has reached a critical point, exposing the Union to supply chain disruptions. Therefore, a considerable effort is being invested to develop local, innovative routes to existing chemicals. Thus, we are currently working on developing an alternative strategy to produce the pharmaceutical building block 5-methylpyrazine-2-carboxylic acid (MPCA), currently used to produce antidiabetic drugs. The original concept was hindered by several problems, such has the toxicity of the product, the short activity of the first enzyme and the high cost of the current substrate. We developed an Escherichia coli able to sustain high concentration of MPCA which is able to produce it form L-threonine, opening the door to the possibility of producing it from cheap substrates like glucose or glycerol.

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s5. Biomedical and Health

Angela Maria Giada Giovenale
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Neurogenesis in Smith-Magenis Syndrome: When Brain Development Go Awry

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[3] UniCamillus - Saint Camillus International University of Health Sciences, Rome, Italy.

SMS, HIPSCS, HINSCS

Smith-Magenis syndrome (SMS) is a rare neurodevelopmental disorder caused by mutations or deletions of the RAI1 gene. Individuals with SMS present a complex clinical picture as intellectual disability, behavioral issues, sleep disturbances, and metabolic defects. To study how RAI1 affects brain development, we generated four human induced neural stem cell lines (hiNSCs) from human induced pluripotent stem cells (hiPSCs)1,2,3 derived from SMS patients, each carrying a different genetic alteration. We evaluated their ability to differentiate into neural cells to detect any possible impairments in neurogenesis. Building on prior findings linking RAI1 haploinsufficiency to abnormal lysosomal acidification and lipid accumulation in SMS fibroblasts 4, we investigated whether similar disruptions occur in neural cells and impact development. These patient-specific models offer a valuable platform to understand SMS mechanisms and explore new therapeutic strategies

1) Giovenale AMG, Turco EM, Mazzoni M, Ferrone I, Torres B, Bernardini L, Vulcano E, Ferrari D, Onesimo R, D'Arrigo S, Zampino G, Pennuto M, De Luca A, Vescovi AL, Rosati J. Generation of the CSSi020-A (14437) iPSC line from a patient carrying a copy number variation (CNV) in the 17p11.2 chromosome region. Stem Cell Res. 2024 Dec;81:103544. doi: 10.1016/j.scr.2024.103544. Epub 2024 Sep 4. PMID: 39260069.
2) Giovenale AMG, Turco EM, Ferrone I, Giacometti C, Tomaselli S, Vulcano E, Ferrari D, Candido O, Bernardini L, De Luca A, Trivieri N, Binda E, Onesimo R, D'Arrigo S, Zampino G, Pennuto M, Vescovi AL, Rosati JD. Generation and characterization of the CSSi021-A (15665) human induced pluripotent stem cell line from a Smith-Magenis syndrome patient with a heterozygous RAI1 mutation. Stem Cell Res. 2025 Aug;86:103726. doi: 10.1016/j.scr.2025.103726. Epub 2025 Apr 26. PMID: 40311325.
3) Altieri F, Turco EM, Vinci E, Torres B, Ferrari D, De Jaco A, Mazzoccoli G, Lamorte G, Nardone A, Della Monica M, Bernardini L, Vescovi AL, Rosati J. Production and characterization of CSSI003 (2961) human induced pluripotent stem cells (iPSCs) carrying a novel puntiform mutation in RAI1 gene, Causative of Smith-Magenis syndrome. Stem Cell Res. 2018 Apr;28:153-156. doi: 10.1016/j.scr.2018.02.016. Epub 2018 Feb 21. PMID: 29494847.
4) Turco EM, Giovenale AMG, Sireno L, Mazzoni M, Cammareri A, Marchioretti C, Goracci L, Di Veroli A, Marchesan E, D'Andrea D, Falconieri A, Torres B, Bernardini L, Magnifico MC, Paone A, Rinaldo S, Della Monica M, D'Arrigo S, Postorivo D, Nardone AM, Zampino G, Onesimo R, Leoni C, Caicci F, Raimondo D, Binda E, Trobiani L, De Jaco A, Tata AM, Ferrari D, Cutruzzolà F, Mazzoccoli G, Ziviani E, Pennuto M, Vescovi AL, Rosati J. Retinoic acid-induced 1 gene haploinsufficiency alters lipid metabolism and causes autophagy defects in Smith-Magenis syndrome. Cell Death Dis. 2022 Nov 21;13(11):981. doi: 10.1038/s41419-022-05410-7. PMID: 36411275; PMCID: PMC9678881.

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A Participatory and Evolutionary Approach to Urban Microbiome Research: Reuniting Microbiology and Society

Giulia Ghisleni[1], Alice Armanni[1], Sara Fumagalli[1], Patrizia di Gennaro[1], Andrea Franzetti[1], Maurizio Casiraghi[1], Massimo Labra[1], Antonia Bruno[1]

[1] University of Milano-Bicocca

MICROBIOME, PARTICIPATORY SCIENCE, BUILT ENVIRONMENTS, URBAN MICROBIOME

Urbanization has disrupted human-microbial relationships, reducing microbiota diversity and contributing to modern health issues. Addressing this requires both scientific research and active public participation. We present two initiatives, Bicocca Sampling Days (BSDs) and UniBiome, that integrate citizen science with microbiome research to explore links between urban environments and human health. BSDs engaged 76 students in collecting over 2,400 environmental samples in Milan, improving their microbiology knowledge and skills. UniBiome, part of the EU-funded MUSA project, involved 160+ students in seasonal sampling of human and environmental microbiomes, revealing how urbanization and lifestyle shape microbial communities. Together, these projects demonstrate how participatory approaches can produce high-quality data while fostering public awareness, offering a scalable model for monitoring and improving microbiome health in urban settings.

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Optimizing culture conditions for biomanufacturing bacterial cellulose and tailoring its functionalization

Martina Dramis[1], Silvia Guerra[2], Luciano Tadiello[2], Luca Giannini[2], Immacolata Serra[1], Paola Branduardi[1]

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BACTERIAL CELLULOSE, POLYMERS FUNCTIONALIZATION, LIPASES

Cellulose, which can be produced with high purity by various bacterial species, can have a highly diverse application, also thanks to its high crystalline structure ensured by intra- and intermolecular hydrogen bonding. Moreover, the modification of its functional groups, key factors for properties tuning, further expand the fields of application of this polymer, for example as reinforcing material.
In this study, Komagataeibacter spp. are used as natural cellulose producing strains. First, alternative substrates have been tested to enhance the production of bacterial cellulose (BC). Secondly, to functionalize the polymer, two routes have been investigated: i) it implies the use of immobilized lipases on BC material; ii) a more innovative method involves the addition to the culture media of a functionalized monosaccharide. Our hypothesis is that the bacteria should be able to incorporate the modified monomer into a forming filament of cellulose, thus directly producing a tuned polymer

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L-Iduronic Acid-Type 1-N-Iminosugars as Pharmacological Chaperones for the Rescue of α-L-Iduronidase in Mucopolysaccharidosis Type I

Lorenzo Taglietti[1], Giuseppe Bonapace[2], Francesca Clemente[3], Daniela Concolino[2], Laura Legnani[1], Maria Teresa Moricca[2], Giuseppe Felice Mangiatordi[4], Maria Giovanna Eva Papadopoulos[4], Michele Pitaro[5], Barbara La Ferla[6]

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IMINOSUGARS, IDUA, CHAPERONES, MPS I, LSDS

Herein we report the synthesis of a series of 1-deoxy-L-idonojirimycin derivatives. This class of compounds has emerged as a promising family of active-site modulators of the lysosomal glycosidase α-L-iduronidase (IDUA).[1] IDUA deficiency is involved in a neurodegenerative lysosomal disorder known as Mucopolysaccharidosis type I.[2] In this context, we describe a novel synthetic strategy for the preparation of a series of analogues of L-iduronic acid. Furthermore, a comprehensive computational conformational analysis, supported by NMR data, revealed that different N-functionalizations can modulate molecular conformation. Finally, preliminary biological evaluation in COS-7 cells exhibited a significant increase in IDUA activity in comparison to the untreated control. This suggests that the compounds are able to recognize and bind their intended target, representing the first evidence of IDUA stabilization through iminosugar-based pharmacological chaperones.[3]

[1] Artola, M.; Kuo, C.; McMahon, S.A.; Oehler, V.; Hansen, T.; van der Lienden, M.; He, X.; den Elst, H.; Florea, B.I.; Kermode, A.R.; van der Marel, G.A.; Gloster, T.M.; Codée, J.D.C.; Overkleeft, H.S.; Aerts, J.M.F.G.. Chem Eur J, 2018, 24, 19081.
[2] Bie, H.; Yin, J.; He, X.; Kermode, A.R.; Goddard-Borger, E.D.; Withers, S.G.; James, M.N.G.. Nat Chem Biol, 2013, 9, 739.
[3] Lin, H.; Chang, S.; Teng, H.; Wu, H.; Li, H.; Cheng, C.; Chuang, C.; Lin, H.; Lin, S.; Cheng, W. Eur J Med Chem, 2023, 247, 115005.

s9. Biomedical and Health

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Identification of miRNA-based biomarkers predictive of lung cancer treatment response and of mechanisms involved in lung cancer progression.

Miriam Kuku Afanga[1], Roberto Cuttano[1], Valentina Melocchi[1], Nicole Di Cillo[1], Francesca Longo[1], Marco Bizzarri[2], Cristiano Carbonelli[3], Paolo Graziano[4], Giovanni Bertalot[5], Paolo Girotti[6], Fabrizio Bianchi[1]

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LUNG CANCER, MICRO-RNAS, BIOMARKERS,

Non-small-cell lung cancer (NSCLC) is the leading cause of cancer-related deaths worldwide, largely due to the lack of effective diagnostic and prognostic biomarkers. MicroRNAs (miRNAs) have recently been implicated in NSCLC progression and therapy resistance. Here, we propose a functional screen of the human miRNome (N=2,580) using a lentiviral overexpression library in relevant lung cancer models. We assess key cancer hallmarks including invasion, migration, proliferation, stemness, immune evasion, and chemotherapy response to identify miRNAs driving these processes. This approach aims to uncover predictive miRNA-based biomarkers and novel molecular targets, potentially guiding the development of alternative therapies for treatment-resistant NSCLC.

1. Cuttano R, Afanga MK, Bianchi F. MicroRNAs and Drug Resistance in Non-Small Cell Lung Cancer: Where Are We Now and Where Are We Going. Cancers (Basel). 2022 Nov 22;14(23):5731. doi: 10.3390/cancers14235731.
2. Montani F, Marzi MJ, Dezi F, Dama E, Carletti RM, Bonizzi G, Bertolotti R, Bellomi M, Rampinelli C, Maisonneuve P, Spaggiari L, Veronesi G, Nicassio F, Di Fiore PP, Bianchi F. miR-Test: a blood test for lung cancer early detection. J Natl Cancer Inst. 2015 Mar 19;107(6):djv063. doi: 10.1093/jnci/djv063. PMID: 25794889.
3. Cuttano, R., Colangelo, T., Guarize, J. et al. miRNome profiling of lung cancer metastases revealed a key role for miRNA-PD-L1 axis in the modulation of chemotherapy response. J Hematol Oncol 15, 178 (2022). https://doi.org/10.1186/s13045-022-01394-1

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Online presentation

Francesca Misitano
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Modulation of Ca2+ handling by combinatorial administration of Istaroxime and Levosimendan in mouse ventricular cardiomyocytes

Francesca Misitano[1], Claudia Maniezzi[1], Corrado Poggesi[2], Gabriella Malfatto[3], Cecilia Ferrantini[2], Antonio Zaza[1], Francesco Lodola[1]

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[3] Division of Cardiology, IRCCS Istituto Auxologico Italiano, Milan, Italy

SERCA2A ACTIVATORS, CA2+ SENSITIZERS, HF, CA2+ HANDLING

Rationale: The effect of combinatorial administration of drugs upregulating SERCA2a and Tn Ca2+ affinity, now available for inotropic therapy, is of practical relevance. Aim: To test the effect of combined SERCA2a enhancement and Tn sensitization by clinically available agents, istaroxime (ISTA) and levosimendan (LEVO) respectively, on intracellular Ca2+ dynamics. Results: As expected, ISTA enhanced SERCA2a-mediated Ca^{2+} reuptake into the SR. LEVO alone unexpected accelerates Ca^{2+} clearance and the effect disappeared after cilostamide pretreatment. When the two drugs were combined the effects were limited to Ca^{2+} clearance (albeit smaller than with ISTA alone), but complemented by a decrease in CaD. Conclusion: The findings can be tentatively interpreted by simultaneous and not complementar SERCA2a activation and increased Ca2+ buffering by Tn. The unexpected LEVO effect may result from enhancement of cAMP-PKA signalling through PDE3 inhibition, a known ancillary effect of the agent.

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Online presentation

Stefano Bianchini
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Anticancer properties of plan extracts on colorectal cancer cell lines

Stefano Bianchini[1], Federica Bovio[1], Francesca Cristani[1], Flavia Guzzo[2], Matilde Forcella[1], Paola Fusi[1]

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COLORECTAL CANCER, DIOSPYROS KAKI, GRATIOLA OFFICINALIS, NATURAL COMPOUNDS, ANTICANCER

Colorectal carcinoma (CRC) is one of the most common types of cancer worldwide. To treat such a heterogeneous disease, many drugs have been developed over the years. However, their efficacy is variable, and their administration may be associated to the insurgence of even strong side effects. Natural compounds present in plants are promising candidates when screening for new drugs, since they have shown numerous anticancer properties in vitro, and represent a reservoir of possible chemotherapeutic agents.
Here, we report that the ethanol extracts derived from Diospyros kaki and Gratiola officinalis have an impact on the E705 and SW480 CRC cell lines, disrupting many hallmarks of cancer cells such as resistance to apoptosis, proliferation and aerobic glycolysis. Therefore, single compounds isolated from these extracts are worth analysing further.

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Istaroxime Prevents AngiotensinII-Induced Remodeling in Pulmonary Artery Smooth Muscle Cells

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PASMCS, ISTAROXIME, ANGII-INDUCED REMODELING, SERCA2, NA^+/K^+ PUMP

Vascular smooth muscle cells (SMCs) undergo abnormal remodeling in response to external stimuli. In particular, Ca^{2+}-dependent pathways are crucially involved in this process. Istaroxime is known to stimulate SERCA2a and inhibit Na^+/K^+ pump in cardiac myocytes. This study investigated istaroxime effects on rat pulmonary artery SMCs (PASMCs) in basal condition and under angiotensin II (AngII)-induced remodeling. Chronic treatment with istaroxime (1 μM, 48 hrs) prevented Ang II-induced PASMCs proliferation by reducing cytosolic Ca^{2+} levels while stimulating Ca^{2+} confinement in the sarcoplasmic reticulum. In particular, istaroxime prevented AngII-induced NFAT-c1 nuclear translocation. Moreover, istaroxime increased SERCA2 protein levels and prevented AngII-induced SERCA2 downregulation. Overall, these results indicate that istaroxime counteracts AngII-induced PASMCs remodeling by promoting SERCA2-mediated Ca^{2+} sequestration, supporting its therapeutic potential in vascular diseases.

s13. Health and Biodiversity

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The built environment and microbiome in human health - insights from everyday life and the hospital environment

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MICROBIOME, HOSPITAL, SKIN, ENVIRONMENT, HUMAN HEALTH

Our lives are influenced by something invisible: the microbiome. It plays a key role in both health and disease[1], and the environment shapes our microbiome while we release microbes into it[2].
To explore the environment–human microbiome connection, we are investigating two complementary settings. First, to trace microbiome exchange during short-term stays in extreme built environments, we collected 731 hospital samples and 231 from patients' hand skin.
Second, to assess how daily exposure and lifestyle influence the microbiome, we collected 213 fecal and 213 urine samples from residents of a Milan district (Italy), along with detailed lifestyle data.
Samples are undergoing DNA extraction and high-throughput microbiome analysis. Preliminary results show that outpatients' skin acquired hospital-associated microbes and vice versa.
Our work has potential implications for infection control, preventive medicine, and urban health policy.

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Functional impact of Toll-like Receptor 4 (TLR4) modulation in lung fibrosis-associated fibroblasts

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TLR4, FIBROSI, IPF, ANTAGONISTS

Idiopathic pulmonary fibrosis (IPF) is a progressive orphan disease characterized by fibrotic changes1. TLR4 has been identified as a central mediator in the fibrotic response, orchestrating crosstalk between immune activation and fibroblast responses2. Preclinical evidences indicate that TLR4 inhibition attenuates fibrosis3. We evaluated the efficacy of two TLR4 antagonists utilizing an in vitro model of pulmonary fibrosis by TGFβ-induced activation of human lung fibroblasts. Our results show a reduction in the expression of fibrotic markers and a partial reversal of the activated fibroblast phenotype following treatment, including ECM production, indicating suppression of the activated state and demonstrating their potential as anti-fibrotic drugs. These findings underscore the role of TLR4 in fibrosis progression and support its potential as a target for therapeutic intervention in lung fibrosis.This approach may offer a new direction for treating IPF and related fibrotic diseases.

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Evaluating Chemotherapeutic Drug Induced Gastro-intestinal Toxicity (DGIT) using a multi-compartimental Gut-on- Chip Model

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MIVO, DYNAMIC FLOW, GUT-ON-CHIP, DRUG INDUCED TOXICITY

The GI tract is a primary drug interaction site, highly susceptible to drug-induced toxicity. Traditional 2D static Caco-2 models fail to mimic complex gut architecture/dynamics. We used the MIVO® Gut-on-Chip, a millifluidic organ-on-chip with Caco-2/HT29 co-culture under double-flow, mimicking luminal and vascular circulation. This enhanced epithelial differentiation, mucus secretion, and tissue functionality. The MIVO® model evaluated GI toxicity of chemotherapies and non-toxic controls. Compounds were applied in concentrations of 1uM, 10uM, 25uM and 100uM. Barrier integrity via TEER was measured at 0h, 4h, 24h, 48h, 96h post-treatment; cell viability also determined. The MIVO® model showed enhanced barrier formation/mucus vs. 2D. Toxic compounds induced TEER reduction (tight junction damage); non-toxic maintained stable TEER/viability. The MIVO® Gut-on-Chip with co-culture/dual-flow offers a more predictive, biomimetic tool for drug-induced GI toxicity.

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Amphiphilic membrane-targeted phototransducers for non-genetic optical stimulation of carciac cell bioelectricity

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OPTOSTIMULATION, CARDIAC ELECTROPHYSIOLOGY, INTRAMEMBRANE PHOTOSWITCHES, CARDIAC CELLULAR MODULATION

The use of light to control cellular activity is emerging as a powerful tool in cell biology, offering minimal invasiveness, high spatiotemporal resolution, and reversibility, thus outperforming conventional stimulation methods. Non-genetic photostimulation exploits exogenous phototransducers to confer light sensitivity. In this context, we introduce two azobenzene-based intramembrane photoswitches, Ziapin2 and MTP2, as candidates for modulating membrane potential in excitable cells.[1] These compounds integrate into the lipid bilayer and modulate V_m without covalent binding or direct ion channel interaction. Ziapin2 induces a mechanical response triggering transient hyperpolarization followed by delayed depolarization, sufficient to elicit action potentials and calcium wave propagation.[2-4] MTP2 electrical photomodulation elicits a light-intensity-dependent sub-threshold depolarization.[5] Together, they offer a proof of concept for optomodulation of cardiac cell excitability.

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Interrogating Amyotrophic Lateral Sclerosis Signatures in TDP-43G376D human induced Neural Stem Cells

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ALS; TDP-43; METABOLISM; HINSCS;

Amyotrophic lateral sclerosis (ALS) is a relentlessly fatal neurodegenerative disease leading to rapid paralysis and death. Increasing amount of evidence show a strong association between mitochondria metabolism disorder and neurodegeneration.
In this study we established a collection of human induced Neural Stem Cells (hiNSCs) lines from asymptomatic, early symptomatic, and late symptomatic individuals carrying the p.G376D TDP-43 mutation. Preliminary findings revealed that hiNSCs carrying TDP-43G376D mutation exhibit enhanced growth rate, increased oxidative stress, mitochondrial dysfunction, and lower ATP production compared to healthy controls. These alterations suggest that molecular perturbations may be rooted in neurodevelopment, potentially increasing the vulnerability of mature neural cells to subsequent degeneration. By investigating the initial dysfunctions, this study aims to provide a platform to unravel critical gaps in understanding the disease onset and progression.

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Cities for pollinators: supporting biodiversity through urban habitats

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URBAN POLLINATORS, MANAGEMENT PRACTICES, BIODIVERSITY ENHANCEMENT

Pollinators enable the reproduction of approximately 80% of wild and cultivated plants, but they are rapidly declining due to human-driven pressures. My PhD research project investigates how urbanisation shapes pollinator communities and explores how urban landscape features and targeted management can enhance pollinator biodiversity. Research was conducted across six Italian cities along an urbanisation gradient, collecting over 8,000 insect samples. Using DNA metabarcoding and morphological approaches, pollinator community structure and plant interactions were identified. A detailed study in Milan assessed the role of urban forests and the effectiveness of management practices, including reduced mowing and the creation of flower strips. Additionally, urban wild bee communities from three European countries were compared with those in natural areas to detect ecological and morphological differences. The results will inform effective pollinator conservation strategies in urban contexts

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Early Insights, Lasting Impact: Mechanistic Enzymology for Characterizing Hit Compound Mechanisms of Action

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DRUG DISCOVERY, ASSAY DEVELOPMENT, MECHANISM OF ACTION, FUNCTIONAL ENZYMOLOGY

High-throughput screening (HTS) identifies diverse hit compounds, but primary assays often yield false positives (interfering compounds, detection system artifacts). Our project focuses on developing innovative secondary assays to unequivocally identify true-positive hits. We pursue two strategies: negative selection via counter-screening and interference assays, and positive selection through orthogonal secondary assays. Integrating mechanistic enzymology early in drug discovery, immediately post-HTS, is crucial. Beyond just IC50 values, we employ diverse biochemical assays to characterize mechanism of action (MOA), including time-dependency, covalent inhibition rates, competitive/non-competitive binding, and association/dissociation kinetics. This comprehensive MOA evaluation provides essential insights, streamlining hit-to-lead and lead-optimization processes and facilitating SAR studies.

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The contribution of the Wiskott-Aldrich Syndrome protein (WASp) to microglial phagocytosis and cytoskeleton dynamics

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NEURODEVELOPMENT; RARE DISEASE; NEUROINFLAMMATION; STEM CELLS

Microglia colonize the brain during embryogenesis and play key roles in shaping neuronal circuits, maintaining homeostasis, and regulating neuroinflammation. These functions depend on cytoskeletal dynamics and phagocytosis. The Wiskott-Aldrich syndrome protein (WASp) regulates cytoskeleton organization and cells maturation in peripheral myeloid cells, but its role in microglia is unknown. We investigated WASp's function in microglial cytoskeletal organization and phagocytosis. Microglia derived from hiPSCs showed active nanoparticle uptake, which was significantly reduced after 1-hour treatment with WASp inhibitors. Immunofluorescence revealed that WASp co-localised with F-actin at membrane ruffles in phagocytic microglia and that inhibition of WASp resulted in an impairment of the cytoskeleton, suggesting its role in maintaining cytoskeletal integrity. To confirm these results, we generated an hiPSC line carrying the R86C missense mutation in the WAS gene for further validation.

s21. Biomedical and Health

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Hijacking the clock: Epigenetic age rewiring via miR-29 modulation.

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AGING, PROSTATE CANCER, MICRORNA, EPIGENETIC REPROGRAMMING

Epigenetic reprogramming has been established as a crucial Hallmark of both cancer and aging1,2. In aged tissues and advanced prostate tumors, DNA methylation deviates from youthful patterns, causing transcriptional shifts, loss of identity, and increased plasticity3. We identified microRNA-29 (miR-29) as the key regulator of the epigenetic machinery, whose levels rise with age and decrease in advanced prostate cancer. Inhibiting miR-29 isoforms can "rejuvenate" healthy fibroblasts, restoring a youthful DNA methylation state characterized by global hypermethylation coupled with targeted promoter demethylation, resulting in a reduction of epigenetic age by several years. These findings indicate that age-related epigenetic alterations foster a permissive environment for oncogenic transformation. By exploiting the inherent reversibility of epigenetic modifications, we aim to develop interventions that both ameliorate age-related dysfunction and impede cancer initiation and progression.

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Neuroprotective effects of plant bioactive compounds on eukaryotic models of Parkinson's disease

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BIOACTIVE MOLECULES, PARKINSON'S DISEASE, NEURODEGENERATION, PLANT BIODIVERSITY, FOOD WASTE VALORIZATION

Within the NBFC project, 64 endemic Italian plant species were screened to identify neuroprotective compounds targeting α-synuclein aggregation, a key hallmark of Parkinson's disease (PD) [1]. Extracts from A. lusitanicum, S. pratensis, V. thapsus, and G. flavum showed strong anti- activity in yeast, SH-SY5Y cells, and in vitro assays. Mass spectrometry identified verbascoside as the major active compound in V. thapsus, capable of directly binding α-synuclein and preventing the formation of toxic oligomers. Furthermore, in collaboration with the "ON Foods" NRRP project, the potential of Glycyrrhiza glabra leaves, typically discarded as an agro-industrial by-product, was investigated for neuroprotective activity. Among its bioactive molecules, pinocembrin showed promising effects. Both verbascoside and pinocembrin are currently being tested in a D. melanogaster PD model to evaluate their efficacy at the organismal level and to support their potential for PD prevention/treatment.

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Exploring the Microbial Biodiversity of Kombucha for Novel Probiotic and Postbiotic Candidates

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KOMBUCHA MICROBIOME PROBIOTIC FERMENTATION DYNAMICS

This PhD project explores the microbial biodiversity of fermented beverages, focusing on kombucha, to identify strains or metabolites with potential probiotic or postbiotic activity. Kombucha is a tea fermented by a symbiotic consortium of bacteria and yeasts (SCOBY). To investigate its microbial ecology, both artisanal and industrial SCOBYs were studied through isolation and identification of culturable microorganisms. Metagenomic analyses are planned to broaden the understanding of community structure and dynamics. Repeated fermentations with different substrates (e.g., chamomile, jujube) were carried out to observe microbial changes. Among the isolates, Zygosaccharomyces bailii was selected for functional characterization. The strain displayed enzymatic activities, sugar metabolism relevant to gut health, and antioxidant and immunomodulatory potential, supporting its possible application as a novel health-promoting agent.

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Modeling Primary Cilium Defects in Joubert Syndrome using iPSC-Derived Neural Stem Cells

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JOUBERT SYNDROME, PRIMARY CILIUM, HINSCS, JOUBERIN

Jouberin is a little-known protein linked to Joubert Syndrome (JS), a rare neurodevelopmental disorder (1). Its role and mechanism in the disease remain unclear. To explore this, we used primary fibroblasts and hiNSCs (2) derived from two JS patients. Analyses revealed altered primary cilium (PC) structure and function, with JS cells showing fewer but longer cilia than controls, along with differences in proliferation and cell cycle progression. A potential cause may be defective PC-mediated sensing of serum changes, impairing PC disassembly and cell proliferation (3). These traits, first observed in fibroblasts, are also confirmed and even amplified in hiNSCs, which provide a more complex and physiologically relevant model. Studying JS in such a system allows deeper insight into the role of Jouberin and the PC during early neurogenesis and neural differentiation. This approach may uncover new mechanisms behind JS and guide future therapeutic strategies.

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s25. Biomedical and Health

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PGM3 Inhibition as a Novel Strategy to Induce BRCAness in HR-Proficient Pancreatic Cancer Cells

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PANCREATIC CANCER , HEXOSAMINE BIOSYNTHETIC PATHWAY, GLYCOSYLATION, DRUG RESISTENCE, DNA DAMAGE

Pancreatic ductal adenocarcinoma (PDAC) is highly lethal, with limited therapeutic options and frequent resistance to gemcitabine (GEM). Metabolic rewiring via the Hexosamine Biosynthetic Pathway (HBP) supports tumor growth and chemoresistance through aberrant glycosylation and modulation of the DNA damage response. Phosphoglucomutase 3 (PGM3), a key HBP enzyme, correlates with poor prognosis and GEM resistance. We investigated FR054, a novel PGM3 inhibitor, in PDAC models. FR054 reduced proliferation, migration, and tumor growth, and synergized with GEM to increase DNA damage and apoptosis. Mechanistically, FR054 impaired ATR/ATM expression, compromised DNA repair checkpoints, and reduced homologous recombination efficiency, inducing a BRCAness phenotype in HR-proficient cells. Targeting PGM3 thus represents a promising strategy to enhance GEM efficacy and overcome resistance in PDAC.

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Bioactive compounds and healthy aging: search for new nutraceutical compounds through the experimental model of chronological lifespan in yeast

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QUERCETIN, GLUCOSINOLATES, COCOA, AGING, YEAST

Quercetin (QUER), glucosinolates (GLSs) and cocoa bean shell extract (CBSE) are bioactive compounds from different natural sources. Despite their structural diversity, they share nutraceutical properties with proven benefits for health [1-3].
We evaluated the impact of QUER, GLSs and CBSE on cellular aging using the Saccharomyces cerevisiae model of chronological aging, which mimics aging in postmitotic mammalian cells [4].
Supplementation with QUER, GLSs, or CBSE at the diauxic shift, a critical metabolic transition marking the beginning of chronological aging, significantly extended lifespan. This pro-longevity effect is mediated through multiple, compound-specific mechanisms, including modulation of central metabolism, nutrient sensing, and autophagy. These findings highlight the potential of QUER, GLSs and CBSE as nutraceuticals for promoting healthy aging and provide mechanistic insights into their cellular targets.

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Wild bees adaptation to urbanization: a multi-Omic approach to implement innovative conservation and ecological transition strategies

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POLLINATORS, MULTI-OMIC, URBANIZATION, ONE-HEALTH

Pollinators are essential to ecosystem functionality, but urban expansion affects their functional diversity, favoring those better adapted to anthropized habitats. We aim to understand strategies they adopt to cope with urban stressors using a multi-omic approach. Our workflow includes genomic, transcriptomic, metabolomic, and DNA metabarcoding data from three wild non-model species collected during two field sessions. The first involved 300 individuals sampled along urbanization gradients in four Italian cities; the second included 180 individuals from colonies reared in urban and natural areas in Milan. Results reveal species-specific genotypic and phenotypic responses to urban stressors, particularly to elevated temperatures and reduced habitat availability. Data integration will support the identification of health and adaptation biomarkers in urban environments, providing tools to evaluate the effectiveness of conservation strategies.

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Investigating the role of the SOWAHC-DIAPH1 complex in physiology and cancer

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MDIA1, ACTIN, LAMELLIPODIA, RUFFLES, SOWAHC

The role of mDia1 in lamellipodia and ruffle formation, driven by branched actin cytoskeleton remodeling, is well established. Through label-free quantitative mass spectrometry, we identified SOWAHC as a novel mDia1 interactor with mDia1-dependent expression. Using a SOWAHC truncation library, we mapped the interaction surface via co-immunoprecipitation. Knock-out HeLa cell models enabled functional studies: DIAPH1 deletion impaired EGF-induced random motility, while SOWAHC loss reduced dextran uptake, indicating defective macropinocytosis. Morphological analyses revealed that, upon EGF stimulation, both knock-outs exhibited reduced protrusion formation. Given the frequent alterations of these genes in cancer, further investigation could inform therapeutic strategies targeting actin-dependent tumor cell behaviors.

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Natural products targeting Amyloid-β aggregation: spectroscopic and biophysical approaches for Alzheimer's disease prevention

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NMR, FTIR, AFM, BIOMOLECULES, METABOLOMICS

Due to the increasing life expectancy, neurodegenerative conditions such as Alzheimer's disease (AD) are becoming more prevalent [1].
Some natural polyphenols, such as flavonoids and catechins, are known for their anti-amyloidogenic and neuroprotective properties [2-4].
Here, myrtle leaf extracts and their phenolic-enriched fractions were prepared and analysed by NMR and LC-HRMS to identify compounds with potential anti-amyloidogenic activity [5], including myricetin and quercetin glycosides, epigallocatechin gallate and ellagic acid.
STD NMR, FTIR and AFM analysis of Aβ1-42 in the presence of extracts and fractions revealed a significant alteration in peptide aggregation, one of the main hallmarks of AD. These findings support the potential of polyphenol-rich myrtle extracts as inhibitors of Aβ pathogenic aggregation and their role in AD prevention.

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Design and 3D fabrication of functional meniscal scaffolds

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ECM, MENISCUS, HYDROGEL, 3D PRINTING, GLYCOSIGNATURE

Menisci are fibrocartilaginous cushions within the knee joint with a highly hydrated ECM and composed of collagen and GAGs. In this study, ECM from paediatric and adult meniscal tissues was compared to investigate their molecular signatures in healthy and damaged conditions. These insights guided the design of a scaffold for meniscal regeneration. To replicate the mechanical properties, a 3D-printed, collagen fibre–like oriented structure was fabricated crosslinking gelatin and hyaluronic acid. Both biopolymers were functionalised with tyramine and the crosslinking was done enzymatically with Horseradish peroxidase. To mimic the biochemical glycosignature, gelatin was previously functionalized with three glycans, D-glucose, D-galactose, and chondroitin sulfate, to enhance the signalling. The morphology of the construct was significantly different depending on the glycosignature. The biological response to these modifications was assessed with hBM-MSCs.

s31. Biomedical and Health

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Multi-omics data analysis to characterize sex-specific metabolic shifts during embryo development

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DYNAMIC METABOLIC MAPS, STEADY-STATE MODELS, MULTI-OMICS DATA INTEGRATION, EMBRYONIC STEM CELLS, SEX-SPECIFIC METABOLIC DISPARITIES

Recent findings suggest that cell metabolism may be key to understanding miscarriages and developmental abnormalities in early embryonic development [1-6]. To explore metabolic differences across pre-, peri-, and post-implantation stages, and between male and female cells, we analyze transcriptomic and metabolomic data from human pluripotent stem cell lines, both embryonic and induced, cultured in naïve 2D and primed 3D conditions. Two independent cell lines per stage and sex were profiled. Transcriptomic data are being used to constrain a core metabolic model via constraint-based sampling (CBS) method [7]. We apply CBS to estimate flux distributions and identify stage- and sex-specific metabolic patterns. Also, metabolomic profiles are being examined to support interpretation of computational results. Particular focus is given to investigating activity in the non-canonical TCA cycle. This integrated approach aims to clarify how metabolism shifts during early human development.

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Online presentation

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The evaluation of Nature-based Solutions through a life-cycle thinking approach: key challenges and opportunities

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ECOSYSTEM SERVICES, INDUSTRIAL ECOLOGY, NATURAL CAPITAL, INTENSIVE GREEN ROOF, SUSTAINABLE PLANNING

Nature-based Solutions (NbS) can solve many urban issues by providing multiple Ecosystem Services (ES). Industrial ecology tools, like Life Cycle Assessment (LCA), have proven to be effective in evaluating NbS, but the integration of ES accounting into LCA is still not systematic. As a case study, an integrated ES-LCA methodology has been modelled to calculate the net environmental benefits and drawbacks of a greening redevelopment. The scope is to identify sustainable and effective urban restoration alternatives for future similar implementations. The LCA has highlighted the most impactful components. Several scenarios have been developed to evaluate possible improvements of deploying alternative materials, for example recycled ones. Moreover, the NbS benefits have been modelled as "ES supply". Finally, the integration of endpoint impacts on ecosystems and positive effects of the greening implementation highlights the importance of species selection in the NbS planning process.

s33. Biomedical and Health

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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, CST COMPLEX

Replication stress poses a significant threat to genome integrity by increasing the vulnerability of replication forks to nucleolytic degradation. In both yeast and humans, the checkpoint kinases Mec1 and Rad53 prevent the generation of deleterious single-stranded DNA through a process that remains poorly understood. Here, we show that the Stn1 subunit of the CST complex cooperates with the checkpoint kinase Mec1 to limit ssDNA generation under replication stress. A Stn1 mutation suppresses the sensitivity to replication stress of Mec1-defective yeast cells and reduces ssDNA levels at stalled forks, whereas both sensitivity and ssDNA accumulation are exacerbated by Stn1 loss of function. Mechanistically, Stn1 counteracts the resection activities of Mre11, Exo1, and Sgs1 by limiting their association not only at stalled replication forks but also at DNA double-strand breaks, revealing that Stn1 functions alongside checkpoint pathways in protecting DNA from nuclease-mediated degradation.

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Posters

p1. Biomedical and Health

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Harnessing Mirror-Image Peptides: Nanoparticle Vectors for Nucleic Acid Delivery in Cancer Treatment

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PEPTIDE-BASED NANOPARTICLES, TARGETED THERAPY, NUCLEIC ACIDS NANODELIVERY, CANCER

The development of efficient delivery systems for nucleic acid-based cancer therapies is an ongoing challenge. Peptide-based systems are emerging as promising strategy due to their tunable properties. Nevertheless, their clinical application is hindered by susceptibility to proteases and limited stability. In this project, we investigate the potential of D-peptides, protease-resistant synthetic peptides composed exclusively of D-amino acids (MIPs, Mirror-Image Peptides), as nanovectors for nucleic acid delivery. Due to their inverted chirality, D-peptides demonstrate remarkable resistance to protease activity while retaining biological functionality. Among various constructs, we selected a promising sequence characterized by the presence of charged amino acids, which enable self-assembling and the complexation of negatively charged nucleic acids (NAs). Using both manual and automated microfluidic-based synthesis we produce nanoparticles complexed with either RNA or double-stranded DNA.

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The role of Collinsella aerofaciens in Non-Communicable Diseases: potential implication in pathogenesis through gut-liver axis activation

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COLLINSELLA AEROFACIENS, GUT MICROBIOTA, NON-COMMUNICABLE DISEASES, INTESTINAL PERMEABILITY, GUT-LIVER AXIS

In recent years, interest in the role of gut microbiota alterations in the pathogenesis of non-communicable diseases (NCDs) has grown significantly. An overgrowth of Collinsella aerofaciens - a bacterium widely present in the gut ecosystem but suggested to act as a pathobiont - appears to be a common feature in individuals with NCDs and may contribute to key mechanisms such as increased intestinal permeability. In this project, C. aerofaciens was isolated from several fecal samples. Molecular fingerprinting was used to identify different genotypes. Unique genotypes underwent shotgun genome sequencing and were compared with strains available in GenBank to reconstruct metabolic pathways and identify molecular determinants involved in the regulation of intestinal permeability and activation of the gut-liver axis. The in vitro characterization of strain-specific effects on intestinal permeability was performed using the TEER assay and gene expression analysis on Caco-2 cell monolayers.

p3. Health and Biodiversity

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Lactic Acid Bacteria, Aromatic Amino Acids and Human Health: Two Functional Approaches

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INDOLES, P-HYDROXYPHENYLLACTIC ACID, LACTIC ACID BACTERIA, AROMATIC AMINO ACIDS

This research explores the metabolic potential of lactic acid bacteria (LAB) in two nutraceutical applications involving aromatic amino acids. The first project aims to develop an iron supplement enriched with a heterofermentative LAB strain producing p-hydroxyphenyllactic acid (HPLA), a tyrosine-derived compound suggested to enhance iron solubility and absorption. The second project focuses on a plant-based fermented food using LAB capable of producing indole derivates, from tryptophan, with potential antihypertensive and immunomodulatory effects. LAB strains were screened for HPLA and indole production and applied to develop functional formulations. In vitro enzymatic assays and cell models will assess effects on iron redox state and hypertension markers, followed by in vivo validation. Together, these projects highlight LAB metabolism of aromatic amino acids as a promising strategy for functional food design targeting key aspects of human health.

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Resolving HSC heterogeneity with integrated single-cell Multi-Omics

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HEMATOPOIETIC STEM CELLS; MULTI-OMICS; GENE THERAPY; COMPUTATIONAL FRAMEWORK.

Hematopoietic Stem Cells (HSCs) are pivotal for cell and gene therapies, but their study is limited by low abundance, poor ex vivo expansion, and challenging in vitro identification. To address this, I developed a bioinformatics workflow integrating scRNA-seq and scATAC-seq on $CD34^+CD90^+$ cells, with additional sorting for CFSE, representing a functional assay, to enrich for slowly proliferating cells, an HSC characteristic. The analysis, implemented through R and Python scripts, aims to identify and characterize human HSCs. Epigenetic profiling revealed additional heterogeneity within the primitive HSC compartment, where transcriptomics alone lacked resolution, suggesting distinct regulatory states. This integrative strategy enhances our ability to characterize HSCs and provides a robust basis for dissecting stem cell states beyond transcriptional profiles alone. The observed diversity may reflect functionally relevant differences in self-renewal and lineage commitment potential.

p5. Industrial Biotech

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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 valuable source of secondary metabolites with pharmaceutical relevance, and the demand for these compounds is continuously increasing. However, traditional production methods—plant extraction and/or chemical synthesis—pose significant sustainability and environmental challenges. Synthetic biology has opened new avenues for the development of alternative production systems. Indeed, combining metabolic engineering with fermentation strategies allows the creation of microorganisms and yeasts as cell factories for the sustainable production of bioactive compounds. In this project, a recombinant Saccharomyces cerevisiae fermentation system is under development to reach the heterologous production of a specific plant natural product, starting from simple and readily available amino acids. This will be achieved through a combined approach involving the heterologous expression of selected enzymes, optimization of metabolic fluxes, and refinement of biotransformation processes.

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Glabranin as a natural modulator of AMPK signaling and lipid metabolism in NAFLD

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STEATOSIS, LIPID METABOLISM, GLABRANIN, AMPK PATHWAY, LIPID DROPLETS

Non-alcoholic fatty liver disease (NAFLD) is a metabolic disorder marked by excessive lipid accumulation and impaired degradation in hepatocytes. In early stages, NAFLD is reversible, and targeting metabolic pathways offers a promising therapeutic strategy. Glabranin, a natural compound from Glycyrrhiza glabra leaves, has anti-inflammatory and antioxidant properties. Here, we evaluate Glabranin's effects on lipid degradation pathways in steatotic HepG2 cells treated with oleic and palmitic acids. Glabranin activated AMPK, reduced lipid droplet accumulation, increased mitochondrial membrane potential, and enhanced resistance to oxidative stress. Kinome profiling revealed activation of kinases involved in metabolic regulation, lipophagy, lypolysis, cell survival, and stress response, supporting Glabranin's role in restoring lipid homeostasis. In conclusion, Glabranin exerts protective metabolic effects in steatotic cells and represents a promising candidate for early-stage NAFLD therapy.

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p7. Biomedical and Health

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Better Together: NMR Spectroscopy and Other Biophysical Tools for the Comprehensive Characterization of Prenylflavonoids Anti-Amyloidogenic Properties

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XANTHOHUMOL, AB1-42, NMR, FTIR, AFM

The major challenge in addressing Alzheimer's disease (AD) lies in the substantial delay between the initiation of the underlying molecular processes and the onset of the first symptoms. As such, the development of primary prevention strategies is of critical importance [1].
In this context, diet has emerged as a promising preventive tool in addressing AD pathogenesis through a multi-targeted approach [2]. Notably, several prenylated flavonoids (PFs) found in different plant families have been shown to inhibit Aβ1-42 peptide aggregation, one of the main hallmarks of AD [3].
Here, we combine NMR spectroscopy with a suite of other biophysical tools for the characterization of the interaction between Aβ1-42 oligomers and three PFs from hops, i.e. xanthohumol, isoxanthohumol, and 8-prenylnaringenin [4]. Among these, xanthohumol can redirect the aggregation of Aβ1–42 towards the formation of amorphous species, thus holding promise as a nutraceutical in the context of AD prevention.

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Design and characterization of an in vitro reconstructed human gut microbiota to model microbe-microbe and host-microbe reciprocal interactions

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

The human gut microbiota (HGM) consists of five bacterial phyla and plays a crucial role in human physiology. HGM functions rely on bacterial metabolites such as short- and branched-chain fatty acids (SCFAs and BCFAs), bacteriocins, and exopolysaccharides (EPS). This project employs an in vitro gut microbiota model composed of a minimal core supplemented with probiotic strains to study microbial interactions and their impacts on the host. The model was tested with fructooligosaccharides (FOS, DP~10). All probiotics use FOS as a carbon source. Genes potentially involved in FOS metabolism in probiotic strains were identified. Probiotic metabolites were tested on HepG2 cells with induced metabolic-associated fatty liver disease (MAFLD), showing reduced lipid accumulation. These preliminary results suggest that selected probiotic strains may have beneficial effects on MAFLD.

p9. Biomedical and Health

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Multi-factor fluid-dynamic model of the tumor microenvironment

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[2] React4life

TUMOR MICROENVIRONMENT, ORGAN-ON-CHIP, ESOPHAGEAL CANCER, BREAST CANCER, MICROPHYSIOLOGICAL SYSTEMS

Recreating the tumor microenvironment (TME) in vitro is essential to develop more predictive cancer models for therapeutic testing. In this study, alginate-based 3D models of breast (MDA-MB-231 cells) or esophageal (OE33 cells) cancer were developed and integrated into a millifluidic system that applies shear forces to mimic in vivo state (flow rate: 0.21 mL/min). Cell viability, proliferation, hypoxia, and migration in the dynamic flow initiating metastasis, were assessed. After 9 days of dynamic culture, both cells formed viable clusters within the hydrogel, with uniform Ki67 expression, indicating sustained proliferation. HIF-1α, often linked to tumor aggressiveness, was detected only in MDA-MB-231 cells under flow, reflecting their more invasive phenotype. Neither cell migrated across the transwell membrane and formed colonies, although a few cells were detected on the membrane. Future improvements will include fibroblasts and endothelial cells to better mimic TME complexity.

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Multidimensional Integrated Quantitative Approach To Assess Safety And Sustainability Of Nanomaterials In Real Case Life Cycle Scenarios Using Nanospecific Impact Categories

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NANOMATERIALS, SSBD, TOXICOLOGICAL DATA ANALYSIS

The European Green Deal promotes the development of innovative, sustainable and safe materials. In this context, the INTEGRANO project, funded by Horizon Europe, aims to assess the safety and sustainability of nanomaterials throughout their life cycle, also through the use of alternative methodologies (NAM) and the Safe and Sustainable by Design (SSbD) approach.
In my first year of PhD, I studied strontium-iron-cerium perovskite nanoparticles designed for membranes intended for wastewater treatment.
The particles, produced by varying two key parameters through Design of Experiments (DoE), were first characterized from a chemical-physical point of view and then tested on human lung epithelial A549 cells to assess oxidative stress, inflammation, cell viability and DNA damage.
This study contributes to the objectives of INTEGRANO, supporting the development of advanced in vitro models and AOP approaches for the assessment of toxic and inflammatory effects of innovative nano(bio)materials.

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Expanding progenitor-like cells via CN-NFAT inhibition to uncover additional differentiation mechanisms

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NFAT, DENDRITIC CELLS, DIFFERENTIATION, CALCINEURIN, STEM CELLS

The NFAT family of transcription factors, regulated by the phosphatase calcineurin (CN), is known for its role in T cells but also influences dendritic cells by promoting terminal differentiation and apoptosis downstream of the LPS–CD14 pathway. We observed that CN–NFAT inhibition in intestinal and neural stem cells led to their expansion in vivo. In a dendritic cell line, CN–NFAT inhibition increased proliferation, induced G2/M accumulation, and promoted a glycolytic, Warburg-like metabolic profile. It also downregulated Sca-1 expression, normally observed at three levels in wild-type cells. Functional assays revealed that Sca-1^low cells were more proliferative, suggesting this marker may stratify cells with different degrees of differentiation. To better characterize these subpopulations we are currently performing scRNA-seq and setting up a genome-wide CRISPR-Cas9 screening to identify key regulators of these phenotypes.

Invited Speakers

is1.

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A journey through intracellular Ca2+ signaling: understanding physiology to interfere with pathology

is2.

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"Life Is good" and other misconceptions. Breve itinerario tra i luoghi comuni e sorprendenti scoperti

Dedicated to PhD Students

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