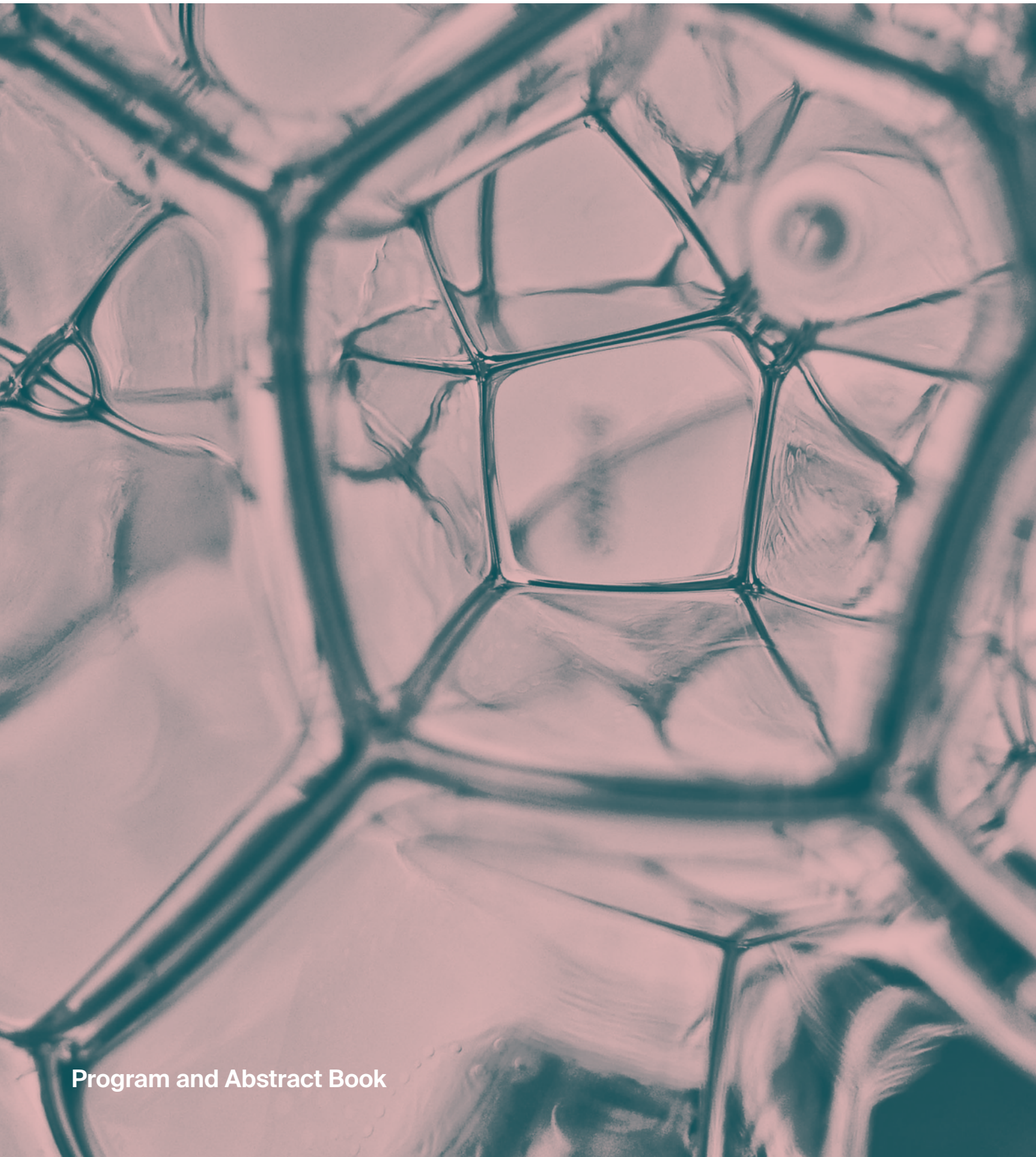
IECM
5th Edition
2026

Conference

The 5th International Electronic Conference on Metabolomics

14–16 October 2026, online



Program and Abstract Book

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14–16 October 2026 | Online

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Welcome from the Chair

We are delighted to welcome you to **The 5th International Electronic Conference on Metabolomics (IECM 2026)**, which will be held online and promoted by the open access MDPI journal *Metabolites* (ISSN 2218-1989; IF 4.5).

In recent years, a series of International Electronic Conferences on Metabolomics (IECM-1, IECM-2, IECM-3 and IECM 2025) have addressed a broad spectrum of topics at the forefront of metabolomics research. The fourth edition, IECM 2025, focused on emerging trends that are transforming the study of metabolic processes, analytical technologies, and systems-level biological insights. Now, **IECM 2026** seeks to explore and discuss the latest advancements in metabolomics within an ever-evolving scientific and technological landscape.

IECM 2026 warmly invites researchers from academia, clinical and industrial sectors to present their original research findings, innovative methodologies, conceptual advances, and new applications in metabolomics. Contributions are welcome in, but not limited to, the following thematic areas:

S1. Lipid and Nutrition Metabolomics;
S2. Ecological and Environmental Metabolomics;
S3. Advanced Data Analysis and Integration in Metabolomics;
S4. Clinical Metabolomics and Drug Metabolism;
S5. Advances in Metabolomics Technologies;
S6. Plant and Animal Metabolism and Metabolic Modeling.

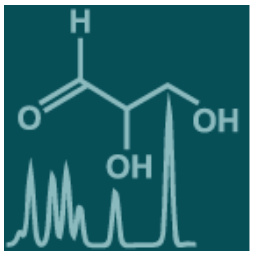
This conference will be conducted entirely in a virtual format, thereby eliminating barriers related to travel and associated expenses for participants across the globe. The online setting provides an inclusive and interactive platform that fosters the timely exchange of cutting-edge research findings, methodological innovations, and emerging concepts in metabolomics and related disciplines.

We extend our sincere appreciation to the global metabolomics community for its continued support, enthusiasm, and engagement. The success of **IECM 2026** depends fundamentally on your active participation and valuable contributions. Your involvement not only enriches the scientific dialogue of our conference, but also enables the timely dissemination of research with impact on the metabolomics field.

Kind regards,
Prof. Dr. Hunter N. B. Moseley
Department of Molecular and Cellular Biochemistry, University of Kentucky, Lexington, USA



Prof. Dr. Hunter N. B. Moseley
Conference Chair
Department of Molecular and Cellular Biochemistry, University of Kentucky, Lexington, USA



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Metabolites (ISSN 2218-1989) is an international, peer-reviewed open access journal of metabolism and metabolomics. Metabolites publishes original research articles and review articles in aspects of metabolites and metabolism relevant to the fields of metabolomics, metabolic biochemistry, computational and systems biology, biotechnology and medicine. We strongly suggest that all submissions have a substantial focus on the measurement, analysis or biological roles of metabolites, metabolic biomarkers or metabolic pathways.

Metabolites encourages scientists to publish their experimental and theoretical results in as much detail as possible. Therefore, there is no restriction on article length. Sufficient experimental details must be provided to enable the results to be accurately reproduced. Electronic material representing additional figures, materials and methods explanation, or supporting results and evidence can be submitted with the main manuscript as supplementary material.

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Session Chairs



Dr. Beate Fuchs

Research Institute for Farm Animal Biology, Core facility Metabolomics & Lipidomics, Dummerstorf, Germany



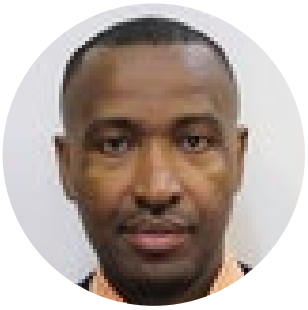
Dr. Bei Gao

School of Environmental Science and Engineering, Nanjing University of Information Science and Technology, Nanjing, China



Prof. Dr. Chi Chen

Department of Food Science and Nutrition, University of Minnesota, St. Paul, USA



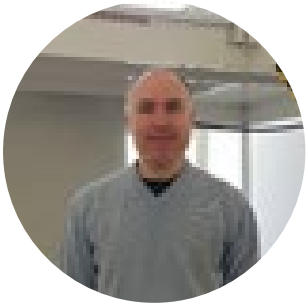
Dr. Fidele Tugizimana

1. Department of Biochemistry, University of Johannesburg, Auckland Park, Johannesburg, South Africa
2. International R&D Division, Omnia Group, Ltd., Johannesburg, South Africa



Prof. Dr. Giuseppe Paglia

School of Medicine and Surgery, University of Milano-Bicocca, Milano, Italy



Prof. Dr. Leonardo Tenori

1. Magnetic Resonance Center (CERM), University of Florence, Sesto Fiorentino, Italy
2. Department of Chemistry "Ugo Schiff", University of Florence, Sesto Fiorentino, Italy



Prof. Dr. Oliver Fiehn

West Coast Metabolomics Center, University of California, Davis, USA



Dr. Reza Salek

School of Clinical Medicine, University of Cambridge, Cambridge Biomedical Campus, Cambridge, UK



Dr. Yunping Qiu

The Einstein-Mount Sinai Diabetes Research Center (ES-DRC), Albert Einstein College of Medicine, NY, USA

Keynote Speakers



Dr. Cecília R.C. Calado

Department of Chemical Engineering, ISEL—Instituto Superior de Engenharia de Lisboa, Instituto Politécnico de Lisboa, Lisbon, Portugal

Cecília R.C. Calado (https://orcid.org/0000-0002-5264-9755 & cecilia.calado@isel.pt) is a Coordinating Professor with Habilitation at the Lisbon Superior Institute of Engineering, Polytechnic University of Lisbon. She is the coordinator of the MSc program in Biomedical Engineering and the R&D Laboratory in Medical Bioengineering. She holds a BSc in Biochemistry (a 5-year university degree), an MSc and a PhD in Biotechnology, and a Habilitation in Biochemistry. Her research combines analytical techniques—used to acquire the molecular fingerprint of biological systems—with machine learning algorithms to develop bioprocess monitoring techniques (in situ, real-time, or high-throughput at-line) as part of Process Analytical Technology (PAT). Additionally, she develops platforms for drug discovery and development, including antibiotics and vaccines, and identifies biomarkers for medical diagnosis and prognosis based on omics.



Dr. David Beale

Environmental Metabolomics and Proteomics, Land & Water, Commonwealth Scientific and Industrial Research Organization (CSIRO), Ecoscience Precinct, Dutton Park, Australia

Dr. David J. Beale is a Senior Principal Environmental Scientist (Science Leader) with the Queensland Government's Department of the Environment, Tourism, Science and Innovation (DETSI) and an Adjunct Professor at Griffith University. He has more than 20 years of experience leading environmental research, multidisciplinary teams, and cross-sector collaborations across government, industry, academia, and communities. Prior to joining DETSI, he spent 18 years at CSIRO, where he led environmental metabolomics research and helped establish the application of omics technologies to environmental science and contaminant assessment. His expertise spans environmental metabolomics, exposomics, functional systems biology, lipidomics, and proteomics, with a focus on understanding the biological impacts of environmental stressors and contaminants. Dr. Beale has developed and applied high-throughput analytical approaches that translate advanced science into practical outcomes for environmental management, risk assessment, regulation, and policy. He currently chairs the Metabolomics Society Environmental Metabolomics (EcoMet) Task Group and the SETAC OMICS Interest Group.



Prof. Dr. Jianguo Xia

Department of Microbiology and Immunology, McGill University, Montreal, Canada

Jianguo (Jeff) Xia is a Professor and Canada Research Chair in Bioinformatics and Big Data Analytics at McGill University. His group develops widely used omics analysis platforms – including MetaboAnalyst, MicrobiomeAnalyst, and OmicsAnalyst – that are widely by 100,000s researchers worldwide, with a focus on metabolomics, microbiomics, and multi-omics integration. A Web of Science Global Highly Cited Researcher every year since 2019, he has published 142 papers (>55,000 citations, H-index 63), trained 60 HQP, and secured $70M in research funding

/



Prof. Dr. Junsong Wang

Center for Molecular Metabolism, School of Environmental & Biological Engineering, Nanjing University of Science & Technology, Nanjing, China



Prof. Dr. Kun Lu

Department of Environmental Sciences and Engineering, University of North Carolina at Chapel Hill, Chapel Hill, USA

Dr. Lu is a Professor in the Department of Environmental Sciences and Engineering at the Gillings School of Global Public Health at the University of North Carolina at Chapel Hill. He also serves as the Scientific Director of the UNC Biomarker Mass Spectrometry Facility. The overarching goal of Dr. Lu's research is to better understand the health effects of environmental exposures, the human exposome, and interindividual differences in response to these exposures. He has extensive expertise in analytical chemistry, microbiome research, and biomarker development. Dr. Lu's laboratory investigates a broad range of environmentally relevant chemicals, including heavy metals, pesticides, and other exposures with significant public health impact. His research has been at the forefront of defining exposure–microbiome–host interactions and establishing the gut microbiome as a critical mediator of the adverse effects of environmental exposures. A major focus of his work is understanding how the gut microbiome interacts with environmental exposures and how the microbiome influences disease susceptibility and health outcomes.



Dr. Laura Righetti

Wageningen University & Research, Wageningen, The Netherlands

Dr. Laura Righetti is Assistant Professor in Analytical Chemistry at Wageningen University and Wageningen Food Safety Research.

She holds a MSc degree in Pharmaceutical Chemistry and Technology from Modena and Reggio Emilia University (IT), a PhD degree in Food Chemistry from University of Parma (IT) obtained in 2017, and postdoctoral experience in Analytical Chemistry at the Justus Liebig University Giessen (DE). Her research interest is focus on small molecules (both natural toxins and bioactive metabolites) and on the development of mass spectrometry based methodologies to comprehensive detect them.

From an analytical chemistry point of view, the comprehensive analysis of secondary metabolites by liquid chromatography–mass spectrometry remains a challenge because of their chemical diversity, the large number of isomeric forms, and the lack of analytical standards. Therefore I have a specific interest in adding innovative analytical techniques such as ion mobility mass spectrometry and mass spectrometry imaging to the metabolomics workflow to overcome the challenge of comprehensively and spatially characterize the "metabolome" in food.



Prof. Dr. Sanjay Swarup

Department of Biological Sciences, Faculty of Science, National University of Singapore (NUS), Singapore, Singapore

Associate Professor Sanjay Swarup is an agriculture and environmental biologist in the Department of Biological Sciences at the National University of Singapore (NUS). He is Deputy Research Director of the Environmental Engineering cluster and Graduate Programme Director at the Singapore Centre for Environmental Life Sciences Engineering (SCELSE), and previously served as Director of the NUS Environmental Research Institute (NERI).

His research combines a background in plant breeding, plant pathology and molecular biology to understand complex agricultural and environmental systems. He leads the Agri-Environmental Systems Biology group, which investigates the mechanistic basis of ecosystem functioning across molecular, organismal and landscape scales, with particular emphasis on phytobiomes, microbiomes and biofilms.

His group studies how microbial communities interact with plants and their surrounding environments through metabolites, metabolic signals and other ecological processes. The research integrates multidisciplinary approaches including metabolomics, metagenomics, computational biology, high-resolution imaging, hydrology, robotics and artificial intelligence. Current research themes include plant–microbiome interactions, crop-associated microbiomes, sustainable agricultural systems, soil management and regenerative agriculture, with the broader aim of developing science-based solutions for food production and environmental sustainability.



Dr. David Beale

1. International Centre for Genetic Engineering and Biotechnology (ICGEB), Cape Town, South Africa
2. International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

Dr Stefano Cacciatore is a Group Leader of the Bioinformatics Unit at the International Centre for Genetic Engineering and Biotechnology (ICGEB) in Cape Town, South Africa. His research focuses on bioinformatics, machine learning, multi-omics, spatial and single-cell transcriptomics, metabolomics, and computational pathology, with particular emphasis on cancer research and African populations. He is the developer of KODAMA and leads the development of computational methods for analysing complex biomedical and high-dimensional datasets. His work combines methodological innovation with translational research in cancers including hepatocellular, pancreatic, prostate, and paediatric malignancies.

Invited Speakers



Dr. Bo Peng

Thrust of Earth, Ocean and Atmospheric Sciences, The Hong Kong University of Science and Technology, Guangzhou, China



Dr. Michele Costanzo

Department of Molecular Medicine and Medical Biotechnology, University of Naples "Federico II", Naples, Italy



Dr. Min Liu

West Coast Metabolomics Center, University of California, Davis, USA



Prof. Dr. Quan-Fei Zhu

School of Biomedical Engineering and Health, Wuhan Textile University, Wuhan, China



Dr. Sonali Mishra

Department of Endocrinology, Metabolism and Lipid Research, Washington University School of Medicine, St. Louis, USA



Dr. Yanqiu Zhou

School of Public Health, Shanghai Jiao Tong University, China

Program Overview

IECM 2026	Day 1 14 October 2026	Day 2 15 October 2026	Day 3 16 October 2026
Morning **9:00–12:00**	**Chair Welcome Speech** **Session 5.** Advances in Metabolomics Technologies	**Session 1.** Lipid and Nutrition Metabolomics	**Session 3.** Advanced Data Analysis and Integration in Metabolomics
Afternoon **14:00–17:00**	**Session 2.** Ecological and Environmental Metabolomics	**Session 4.** Clinical Metabolomics and Drug Metabolism (15:00-18:00 CEST)	**Session 6.** Plant and Animal Metabolism and Modeling **Chair Closing Speech**

IECM Program

14 October 2026 (Wednesday)

Session 5. Advances in Metabolomics Technologies

Time: 9:00 (CEST) | 3:00 (EDT, New York) | 15:00 (CST, Asia, Beijing)

Time in CEST	Speaker	Title
9:00–9:05	**Prof. Dr. Hunter Moseley** Opening Remarks	
9:00–9:05	**Prof. Dr. Leonardo Tenori** Opening Remarks	
9:05–9:30	**Dr. Stefano Cacciatore** Keynote Speaker	Title to be announced
9:30–9:50	**Dr. Michele Costanzo** Invited Speaker	Metabolomics as a Lens into Sex Differences
9:50–10:10	**Prof. Dr. Quan-Fei Zhu** Invited Speaker	Emerging Analytical Strategies for FAHFA Characterization in Metabolomics
10:10–10:25	**Desta Gebremedhin Gebrehiwot** Selected Speaker	Valorization of Rugulopteryx okamurae through the elaboration of bioactive-rich and functional extracts: Optimization of extraction conditions and comprehensive characterization by complementary spectrophotometric and metabolomics tools
10:25–10:40	**Marlene Nyambura Thaitumu** Selected Speaker	Volumetric Absorptive Microsampling in Biomarker Analysis: Insights from Targeted and Rapid Microbore Metabolic Profiling Approaches
10:40–10:55	**Valentina Giraldi** Selected Speaker	Lyophilization-based protocol for human plasma and serum metabolomics by benchtop NMR spectroscopy: optimization and validation
10:55–11:10	**Gaia Meoni** Selected Speaker	Fluorine-Tagging Strategies for Amino Acid Detection by Low-Field ^{19}F NMR Spectroscopy
11:10–11:25	**Monica Trif** Selected Speaker	Integrating Metabolomics into the Development of Functional Bee-Based Foods for Healthy Ageing
11:25–11:40	**Pinky Kain** Selected Speaker	High-resolution spatiometabolomics in Drosophila: Advancing tissue-specific metabolomics via DESI-Mass Spectrometry Imaging
11:40–12:00	**Dr. Sonali Mishra** Invited Speaker	The Role of Metabolomics in Advancing Rare Disease Research

Time: 14:00 (CEST) | 8:00 (EDT, New York) | 20:00 (CST, Asia, Beijing)

Time in CEST		Title
14:00–14:05	**Dr. Bei Gao** Opening Remarks	
14:05–14:30	**Dr. David Beale** Keynote Speaker	From Molecules to Ecosystems: The Power of Environmental Metabolomics
14:30–14:55	**Prof. Dr. Sanjay Swarup** Keynote Speaker	Chemical Dialogues in Rhizosphere Ecology: Plant Volatiles and Microbial Sulfur Signals
14:55–15:20	**Prof. Dr. Kun Lu** Keynote Speaker	Novel Metabolomic Strategies for Decoding the Exposome
15:20–15:40	**Dr. Min Liu** Invited Speaker	Functional Exposomics: Decoding Mechanisms and Drivers of Human-Relevant Chemical Mixture Effects.
15:40–16:00	**Dr. Yanqiu Zhou** Invited Speaker	Prenatal Exposome of Tire-Derived Chemical Mixtures: Integrating Metabolomics to Identify Key Environmental Drivers of Early-Life Health
16:00–16:20	**Dr. Bo Peng** Invited Speaker	Human Exposome Biomonitoring: Biofluid Matrix Selection and Exposure Biomarker Discovery

16:20–16:35	**Luciana de Jesus Jatoba** Selected Speaker	Comparative Analysis of Sample Preservation Techniques for Plant Ecometabolomic Studies
16:35–16:50	**Willian Garcia Birolli** Selected Speaker	Metabolite identification of alpha-cypermethrin biodegradation by citrus bacteria

15 October 2026 (Thursday)

Session 1. Lipid and Nutrition Metabolomics Technologies

Time: 9:00 (CEST) | 3:00 (EDT, New York) | 15:00 (CST, Asia, Beijing)

Time in CEST	Speaker	Title
9:00–9:10	**Prof. Dr. Giuseppe Paglia** Opening Remarks **Dr. Beate Fuchs** Opening Remarks	
9:10–9:35	**Dr. Laura Righetti** Keynote Speaker	The Good and the Bad: Non-Targeted approaches for unraveling the complexity of food metabolome
9:35–9:50	**Yongting Luo** Selected Speaker	Breast Milk Oxylipin Signature Predicts Infant Gut Microbiota Maturation: A Prospective Lipidomics–Metagenomics Cohort Study
9:50–10:05	**Sadaqat Ali** Selected Speaker	Astaxanthin Supplementation Mitigates Chronic Heat Stress-Induced Dysregulation of Glycerophospholipids and Sphingolipids in Broiler Thigh Muscle: Untargeted LC-MS Lipidomics Evidence
10:05–10:20	**Rajesh Babu Komaragiri** Selected Speaker	Integrated Metabolomics, Network Pharmacology, and Cell-Based Validation of Indigenous Rice Bran Cultivars against Colorectal Cancer Chemoprevention
10:20–10:35	**Cheetra Bhajan** Selected Speaker	Metabolite Profiling of Selected Mauritian Endemic Fruits
10:35–10:50	**Simone Serrao** Selected Speaker	Immune-cell metabolomics in frailty reveals mitochondrial dysregulation potentially linked to functional vitamin B12 deficiency
10:50–11:05	**Marina Hernández Martín** Selected Speaker	Dietary Grape Pomace Polyphenols Modulate Hepatic Fatty Acid Metabolism in Early Diet-Induced MASLD
11:05–11:20	**Marta Nobile** Selected Speaker	Personal Urinary Metabotypes and Sex Differences Dominate Seasonal and Dietary Effects in a Four-Season Longitudinal Urine Metabolomics Study
11:20–11:35	**Rúben J. Moreira** Selected Speaker	"The testis remembers": lifestyle-based weight loss partially rescues fertility despite testicular metabolic memory of early-life obesity
11:35–11:50	**Ujjalkumar Das** Selected Speaker	The EV–Oxylipin Axis in Atherosclerosis: Characterization of oxylipin cargo in plasma-derived extracellular vesicles from Ldlr-/- mice

Session 4. Clinical Metabolomics and Drug Metabolism

Time: 15:00 (CEST) | 9:00 (EDT, New York) | 21:00 (CST, Asia, Beijing)

Time in CEST	Speaker	Title
15:00–15:05	**Dr. Yunping Qiu** Opening Remarks	
15:05–15:30	**Dr. Cecília R.C. Calado** Keynote Speaker	Metabolomics fingerprinting based on FTIR spectroscopy for biomarkers discovery
15:30–15:45	**Xinhui Wang** Selected Speaker	From Plasma Metabolites to Therapeutic Targets: Translational Prioritization of Metabolic Pathways in Intervertebral Disc Degeneration
15:45–16:00	**Ashwini V Rao** Selected Speaker	Cord Blood Metabolomic Profiling Reveals Fetal Reprogramming in Intrauterine Growth Restriction
16:00–16:15	**Amrita Sahu** Selected Speaker	Investigation of Metabolic Dysregulation in Advanced-Stage Chronic Kidney Disease Using NMR-Based Urinary Metabolomics
16:15–16:30	**Elizaveta Yakunina** Selected Speaker	Ventilator-Associated Pneumonia and Aromatic Microbial Metabolites in Patients After Ischemic and Hemorrhagic Stroke
16:30–16:45	**Maria Bora Salobehaj** Selected Speaker	Characterization of Intra- and Extracellular Metabolic Profiles by ^{1}H NMR in Aβ1-42-Treated Human Astrocytes from Healthy and Alzheimer's Disease Subjects

16:45–17:00	**Prof. Ilse du Preez** Selected Speaker	Post-therapy metabolic profiles of tuberculosis patients with treatment-cured and treatment-failed outcomes
17:00–17:15	**Alexia K Lo** Selected Speaker	Development and Validation of a Comprehensive LC-MS/MS Targeted Assay for Uremic Solute Profiling in Chronic Kidney Disease
17:15–17:30	**Arjun Sengupta** Selected Speaker	Neurobehavioral Sensitization to Sleep Deprivation is Associated with Re-organization of Circadian Metabolic Rhythm
17:30–17:45	**Mariana Duarte** Selected Speaker	Quality control of the culture media during early stages of NK-cell expansion process

16 October 2026 (Friday)

Session 3. Advanced Data Analysis and Integration in Metabolomics

Time: 9:00 (CEST) | 3:00 (EDT, New York) | 15:00 (CST, Asia, Beijing)

Time in CEST	Speaker	Title
9:00–9:10		**Prof. Dr. Oliver Fiehn** Opening Remarks **Dr. Reza Salek** Opening Remarks
9:10–9:35	**Prof. Dr. Jianguo (Jeff) Xia** Keynote Speaker	Multi-Modal and Multi-Omics in MetaboAnalyst: From Static Statistics to Context-Aware Interpretation
9:35–10:00	**Prof. Dr. Peter D. Karp** Keynote Speaker	Title to be announced
10:00–10:15	**Huaxu Yu** Selected Speaker	MassCube: a Python framework for end-to-end metabolomics data processing from raw files to phenotype classifiers
10:15–10:30	**Chenxin Duan** Selected Speaker	A structure-aware platform for comprehensive lipidomics annotation and quantification
10:30–10:45	**Joe Lomax** Selected Speaker	Penalised Mixed Effects Modelling of Longitudinal Metabolomics Data
10:45–11:00	**Parisa Shahnazari** Selected Speaker	Toward Interpretable Multi-Omics Biomarker Discovery in Breast Cancer: A Meta-Analytic Framework Integrating Attention-Based Deep Learning, Deep Transfer Learning, and Contrastive Learning
11:00–11:15	**Paula Barciela Álvarez** Selected Speaker	Mapping phytochemicals and neuroprotective mechanisms in five medicinal plants: a knowledgebase-driven approach
11:15–11:30	**Daniel Boehmler** Selected Speaker	Enabling subcellular DESI-MSI for broad adoption: Acquisition through to analysis
11:30–11:45	**Robert M Flight** Selected Speaker	Quality-Control and Quality-Assessment of Metabolomics Workbench
11:45–12:00	**Mario A Flores** Selected Speaker	TG-ME-Met: An Integrative Transformer-Graph Variational Autoencoder Framework for Multi-Modal Characterization of Tumor Microenvironments through Spatial Transcriptomics and Metabolomics

Session 6. Plant and Animal Metabolism and Modeling

Time: 14:00 (CEST) | 8:00 (EDT, New York) | 20:00 (CST, Asia, Beijing)

Time in CEST	Speaker	Title
14:00–14:10		**Prof. Dr. Chi Chen** Opening Remarks **Dr. Fidele Tugizimana** Opening Remarks
14:10–14:35	**Prof. Dr. Junsong Wang** Keynote Speaker	Title to be announced
14:35–14:50	**Yan Cheng** Selected Speaker	A multifunctional ANL superfamily gene OsACS couples oxylipin and phenylpropanoid metabolism
14:50–15:05	**Aleena Parvez** Selected Speaker	Metabolic Profiling and Biochemical Diversity of the Cucurbitaceae Family: Implications for Agricultural and Nutritional Optimization
15:05–15:20	**Ashruti Fulmali** Selected Speaker	Metabolomic profiling reveals Hydrogen sulfide-induced alterations in the secondary metabolite production of Trigonella foenum-graecum (Fenugreek).
15:20–15:35	**Maria Almeida-Santos** Selected Speaker	Metabolomic characterisation of the testis in Lysosomal Acid Lipase–deficient mice highlights age-dependent changes in energy- and lipid-associated metabolites
15:35–15:50	**Alfred O. Onefeli** Selected Speaker	Comparative Secondary Metabolite Profiles and FTIR-Based Chemical Fingerprinting of Three Vernonia Species in Nigeria

15:50–16:05	**Karliane Pinto Viana** Selected Speaker	LC-MS/MS-Based Metabolomic Profiling and Antioxidant Potential of Combretum mellifluum Flower Extracts
16:05–16:20	**Juan José Romero-Tovar** Selected Speaker	Untargeted metabolomics reveals phenology and cultivation-dependent signatures of vasodilatory activity in Heliopsis longipes leaves
16:20–16:30	**Prof. Dr. Hunter Moseley** Closing Remarks	

Poster List

Submission ID	Author	Title
Session 1. Lipid and Nutrition Metabolomics		
Sciforum-203067	Boda Damodar, Vishal Verma, Vishal Gill, Avinash Kumar, Shailendra Pratap Singh*	Nutrient-Dense Wheatgrass Ladoo Formulations for Athlete Nutrition: A Biochemical Profiling of Sunflower and Pumpkin Seed Variants
Sciforum-206939	Georgios Theodoridis*, Theano Rizou, Pol Giménez Gil, Artemis Vasileiou, Christina Virgiliou*	Lipidomic Profiling of Egg Yolk to Evaluate Alternative Protein Sources in the Mediterranean Diet
Sciforum-190842	Giovanni Aulisa, Isaac Amoah, Mauro Lombardo*	Diet–Microbiota–Metabolome Interactions: The Role of Trimethylamine-N-Oxide (TMAO) as a Nutritional Metabolomics Biomarker in Humans
Sciforum-205906	Marina Santana*, Amanda Guimarães de Araújo, Eder H. A. Pinto, Artur Fernando A.M. Oliveira, Jackson Monteiro, Vanessa Vendramini	NUTRACEUTICAL EFFECT OF AÇAÍ ON SPERM FUNCTION IN THE D-GALACTOSE-INDUCED AGING MODEL IS NOT LINKED WITH GLYCOLYSIS PATHWAY METABOLOMICS
Sciforum-204584	Luan da Silva Dias Rabelo*, Álex Aparecido Rosini Silva, Andréia de Melo Porcari, Ana Lúcia Tasca Gois Ruiz, Mary Ann Foglio	LC-MS-Based Metabolomic Characterization of an Unsaponifiable Bixa orellana Fraction Before and After Tocotrienol Enrichment
Sciforum-195125	Parham Jalali*, Navid Moravej, Aida Mohammadi, Alireza Shirin, Javad Mehrabani, Hadi Nobari	Skeletal Muscle Metabolomics and Targeted Lipidomics of the Gluteus Maximus Following Acute Eccentric-Overload Exercise: An Exploratory Pilot Study
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Session 1. One Health Approaches to Emerging Zoonotic Threats

Sciforum-165518: Nutrition Metabolomics and Cognitive Health: A Systematic and Integrative Review

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Introduction: Cognitive decline and neurodegenerative disorders represent major global health challenges, with nutrition recognized as a potentially modifiable factor influencing brain health across the lifespan. Nutrition metabolomics enables the identification of diet-derived and endogenous metabolites associated with cognitive function. However, evidence remains heterogeneous across populations, dietary exposures, analytical platforms, and cognitive assessments. This systematic and integrative review aimed to synthesize evidence on metabolomics-based biomarkers linking nutrition to cognitive health.

Methods: PubMed, Scopus, and Web of Science were systematically searched for studies published between January 2010 and December 2025, following PRISMA guidelines. Eligible studies included human observational or intervention research applying metabolomics or lipidomics to examine associations between dietary exposures, biological metabolites, and cognitive outcomes. Animal studies, reviews, conference abstracts, studies without cognitive assessment, and investigations not using metabolomic or lipidomic approaches were excluded. Methodological quality was assessed using appropriate critical appraisal tools according to study design. Because of substantial heterogeneity in study designs, populations, analytical platforms, dietary assessments, and cognitive measures, findings were synthesized qualitatively through an integrative approach.

Results: Thirty-seven studies met the eligibility criteria. Recurrent metabolic signatures associated with cognitive performance involved polyunsaturated fatty acids, phospholipids, sphingolipids, amino acids, and gut microbiota-derived metabolites. Diets rich in omega-3 fatty acids, polyphenols, and plant-based foods were generally associated with favorable metabolic profiles and better cognitive outcomes. Conversely, Western dietary patterns were more frequently linked to pro-inflammatory and potentially neurotoxic metabolite signatures. Lipid metabolism, oxidative stress, and neuroinflammatory pathways were the most consistently reported mechanisms.

Conclusions: Available evidence suggests that nutrition-related metabolic pathways are associated with cognitive health and may support the identification of biomarkers for cognitive decline. Nevertheless, methodological heterogeneity limits comparability and causal interpretation. Standardized analytical procedures, longitudinal designs, and multi-omics integration are needed to improve reproducibility and translational relevance.



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Sciforum-179720: Breast Milk Oxylipin Signature Predicts Infant Gut Microbiota Maturation: A Prospective Lipidomics–Metagenomics Cohort Study

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Introduction: Breast milk provides essential lipids shaping the infant gut microbiome, but the role of bioactive oxidized lipids (oxylipins) remains unknown. This study investigates whether breast milk oxylipins predict early-life gut microbiota maturation.

Methods: In a prospective cohort of 95 mother-infant dyads, breast milk samples were collected at 1, 3, and 6 months postpartum. Oxylipins were profiled using ultra-high-performance liquid chromatography–tandem mass spectrometry (UHPLC-MS/MS) targeting 56 oxylipins from the COX, LOX, and CYP pathways. Infant fecal metagenomes were sequenced (shotgun) at corresponding time points. Data on delivery mode (vaginal/C-section), maternal and infant antibiotic exposure (yes/no, timing), maternal diet (food frequency questionnaire), and feeding practices (exclusive/predominant/partial breastfeeding) were collected and included as covariates. Multi-omics integration was performed using sparse partial least squares (sPLS) regression with adjustment for these confounders.

Results: Among 42 detected oxylipins, 12,13-DiHOME, 9,10-DiHOME, and 5-HETE emerged as the strongest predictors (VIP score >1.8) independent of confounders. Infants in the high-DiHOME cluster exhibited accelerated microbiota maturation, with a 2.4-fold higher *Bifidobacterium* dominance ($p<0.001$) and increased α-diversity (Shannon index: 3.2 vs. 2.1, $p<0.01$) by 3 months. These oxylipins correlated with upregulation of bacterial CAZymes involved in HMO utilization ($r=0.68$, $p<0.001$). The oxylipin signature explained 47% of the variance in gut microbial composition at 6 months, outperforming traditional lipid classes (triglycerides, phospholipids). Infants with a “pro-maturation” oxylipin profile had significantly lower incidence of colic and atopic dermatitis at 12 months (OR=0.31, 95% CI: 0.15–0.64).

Conclusions: This study identifies a novel breast milk oxylipin signature—12,13-DiHOME and 5-HETE—that predicts infant gut microbiota maturation and immune outcomes, revealing a previously unrecognized role of dietary oxylipins in early-life microbial programming.



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Sciforum-190842: Diet–Microbiota–Metabolome Interactions: The Role of Trimethylamine-N-Oxide (TMAO) as a Nutritional Metabolomics Biomarker in Humans

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Introduction:

Trimethylamine-N-oxide (TMAO) is a gut microbiota-derived metabolite increasingly studied as a biomarker linking diet, host metabolism, and cardiometabolic health. It is produced from dietary precursors such as choline, betaine, and L-carnitine, making it a key component of the diet–microbiota–metabolome axis.

Methods:

A literature review was conducted to assess how dietary patterns influence circulating and urinary TMAO levels in humans. Studies were retrieved from PubMed, Scopus, and Cochrane databases up to July 2026. Eligible studies were original human research examining TMAO in relation to diet interventions or patterns. Out of 447 records, 31 studies met the inclusion criteria and were analyzed qualitatively, considering study quality and methodological limitations.

Results:

Dietary patterns strongly influence TMAO concentrations, supporting its role as a metabolomic marker of diet-related metabolic responses. Plant-based diets (Mediterranean, vegetarian, vegan, DASH) are generally linked to lower TMAO levels, while diets rich in red meat and animal products tend to increase them. Weight loss and caloric restriction are also associated with reduced TMAO. Intervention studies show that TMAO levels can change rapidly with dietary modifications. However, the relationship is complex: increases in TMAO have been observed after consuming foods considered cardioprotective, such as fish and whole grains. This suggests that elevated TMAO is not always indicative of unhealthy diets. Inter-individual variability, influenced by host and microbial factors, further complicates interpretation, and gut microbiota composition alone does not fully predict TMAO production.

Conclusions:

TMAO is a promising biomarker in nutritional metabolomics for studying interactions between diet, gut microbiota, and metabolism. While responsive to dietary changes, its interpretation in cardiometabolic risk requires caution, as its role depends on dietary context, host characteristics, and microbial activity. More longitudinal and controlled studies integrating metabolomic, microbiome, and clinical data are needed to clarify its biological significance and potential in precision nutrition.



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Sciforum-194457: Immune-cell metabolomics in frailty reveals mitochondrial dysregulation potentially linked to functional vitamin B12 deficiency

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Frailty is a multifactorial condition of reduced physiological reserve and increased vulnerability to adverse health outcomes, in which nutritional deficiencies play a central but underestimated pathophysiological role. While most metabolomics studies in frailty focused on plasma or serum, the intracellular metabolism of immune cells remains unexplored. This study applied untargeted metabolomics and lipidomics to peripheral blood mononuclear cells (PBMCs) and their subpopulations, T lymphocytes (CD3+) and monocytes (CD14+), isolated from elderly subjects to identify metabolic variation associated with frailty.

In 82 subjects aged $>$65 years frailty and multimorbidity were assessed according to Fried criteria, and considering the presence of at least two chronic diseases, respectively. Participants were categorized as Non-Frail (NFWoM), Frail without multimorbidity (FWoM), and Frail with multimorbidity (FrailtyWM). Cell populations were isolated from whole blood by density gradient centrifugation and immunomagnetic separation. Metabolites and lipids were extracted using methanol-based protocol and analyzed by UHPLC-Q-TOF.

CD14+ captured the most robust metabolic signatures of frailty. FWoM showed increased glycolytic intermediates, energy metabolites, acylcarnitines, and antioxidant-related compounds, alongside enrichment of glycolysis, TCA cycle, and β-oxidation, with respect to NFWoM. Methylmalonic acid (MMA) was markedly elevated in FWoM, suggesting a metabolic pattern compatible with vitamin B12 deficiency via impaired methylmalonyl-CoA mutase. Together with increased 2-hydroxyglutarate and 1-methylnicotinamide, MMA may also reflect mitochondrial dysfunction and pseudohypoxic, pro-inflammatory phenotype. FrailtyWM group showed a similar but attenuated profile. Lipidomics revealed in both frailty groups increased concentration of structural phospholipids and plasmalogens, and depletion of triacylglycerols and fatty acids, indicating membrane remodeling, antioxidant adaptation, and enhanced lipid catabolism.

This study provides the first integrated metabolomic and lipidomic characterization of immune cell subpopulations in frailty, identifying CD14+ as the most informative cell type, and MMA as potential marker linking vitamin B12 deficiency, mitochondrial and metabolic decline, to be explored in future clinical studies.



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Sciforum-195125: Skeletal Muscle Metabolomics and Targeted Lipidomics of the Gluteus Maximus Following Acute Eccentric-Overload Exercise: An Exploratory Pilot Study

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introduction: The gluteus maximus is a major locomotor and metabolic organ, yet characterization of its tissue-level metabolomic response to acute mechanical stress remains limited. This exploratory pilot study utilized integrated muscle metabolomics and targeted lipidomics to profile the acute post-exercise biochemical alterations in GM tissue following a single bout of eccentric-overload exercise with post-workout carbohydrate-protein versus carbohydrate-only ingestion.

Methods: In a randomized, double-blind nutritional allocation design, 20 healthy, resistance-trained men (n = 10/group) performed an acute EO session (5 sets of 10 flywheel hip extensions), immediately followed by either a carbohydrate-protein hydrolysate (CHO+PRO) or a carbohydrate-only (CHO) beverage. To capture early-phase metabolic and transcriptional responses, percutaneous muscle biopsies of the GM were obtained 3 hours post-exercise. Pre-exercise baseline biopsies were not obtained in this pilot study to minimize participant burden. Flash-frozen tissue specimens underwent polar metabolite and hydrophobic lipid extraction for UHPLC-MS/MS profiling. To minimize overfitting, unsupervised Principal Component Analysis (PCA) and univariate ANOVA with Benjamini-Hochberg FDR correction ($q < 0.05$) were utilized, supplemented by cross-validated OPLS-DA with permutation testing. Localized Interleukin-6 (IL-6) mRNA expression was quantified via RT-qPCR.

Results: Univariate and multivariate profiling identified significant alterations in 11 muscle metabolites and lipid species between groups. The CHO+PRO cohort exhibited a distinct accumulation of branched-chain amino acids (leucine and isoleucine), alongside elevated levels of specific long-chain acylcarnitines (palmitoylcarnitine and oleoylcarnitine) and tricarboxylic acid cycle intermediates (succinate and malate). This intracellular pattern was associated with IL-6 mRNA expression. These preliminary findings suggest altered intermediary substrate utilization within muscle tissue during the early recovery phase.

Conclusions: Acute post-exercise protein-carbohydrate co-ingestion was associated with distinct exploratory shifts in the acylcarnitine and amino acid profiles of the GM 3 hours following EO stress. Given the small sample size and absence of baseline metabolomic data, these findings should be interpreted cautiously. Nevertheless, they provide preliminary molecular signatures that may inform future dynamic metabolic flux-based studies.



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Sciforum-195584: Himalayan Geography Imprints the Metabolome of Traditional Yak Milk Churupi: A Multi-Region Comparative Study

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Churupi, a hard acid-coagulated fermented yak milk (Bos grunniens) product, is produced under widely contrasting agro-climatic conditions across the Himalayas, from the cold, arid, hypoxic Ladakh (3,000–5,500 m a.s.l.) to the temperate, humid highlands of Arunachal Pradesh and Darjeeling (2,000–4,500 m a.s.l.). While compositional studies on Churupi exist, untargeted metabolomics linking geographical origin to stress-adaptive metabolic signatures and biofunctional potential remains unexplored. Three independent Yak milk Churupi from each geographical region,Ladakh (LDK), Arunachal Pradesh (AP), and Darjeeling (DJ), with cow milk Churupi as control, were subjected to untargeted GC-MS metabolite profiling. A total of 80 metabolites were identified, of which 28 were statistically significant. Multivariate analysis including PCA and hierarchical clustering were performed using MetaboAnalyst 6.0. Biofunctional assessment included in vitro gastrointestinal digestion, DPPH radical scavenging, and ACE inhibitory activity. PCA clearly separated LDK from eastern Himalayan samples, with all yak Churupi distinct from cow milk control. LDK Churupi had greater abundance of gluconic acid, D-galactopyranose, proline, 5-oxoproline and N-acetyl-D-glucosamine metabolites consistent with metabolic adaptation to cold, high-altitude environments.AP and DJ Churupi were enriched in 2,3-butanediol, 2-hydroxy-3-methylbutyric acid, 2-hydroxyisocaproic acid and hexanoic acid consistent with enhanced pyruvate fermentation, branched-chain amino acid metabolism and flavour-associated microbial activity.After simulated GI digestion, LDK Churupi had the highest DPPH scavenging (73.27%) and ACE inhibition (68.12%) which were substantially higher than AP, DJ and control ($p < 0.05$). The findings suggest that Himalayan geography is associated with distinct metabolomic profiles in traditional yak milk Churupi. The metabolomic signature of LDK Churupi, potentially influenced by high-altitude agro-climatic conditions, was associated with enhanced antioxidant and ACE inhibitory activities following simulated gastrointestinal digestion. These results support the application of geographical metabolomics for the characterization, valorisation and authentication of traditional Himalayan fermented dairy products.



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Sciforum-195836: Integrated Metabolomics, Network Pharmacology, and Cell-Based Validation of Indigenous Rice Bran Cultivars against Colorectal Cancer Chemoprevention

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In Ayurveda, indigenous rice cultivars are highly regarded, with pigmented landraces described as Rasāyana formulations known for rejuvenating properties. Despite their ethnopharmacological significance, molecular mechanisms underlying their role in colorectal cancer (CRC) prevention remain poorly understood. This study employed an integrated approach combining metabolomics, network pharmacology, and cell-based validation to explore the CRC chemopreventive potential of indigenous rice bran cultivars.

Rice bran samples from seven pigmented and two non-pigmented cultivars were sequentially extracted. Methanolic extracts demonstrated superior phytochemical enrichment and antioxidant activity, evidenced by FRAP, DPPH, and ABTS assays, with pigmented cultivars exhibiting higher bioactivity. Initial untargeted LC–MS/QTOF metabolomics identified 25,000 features, refined to 1,554 reproducible metabolites. Multivariate analyses separated pigmented from non-pigmented cultivars, identifying 146 significantly altered metabolites and 17 putative rice bran biomarkers.

Network pharmacology identified seven bioavailable metabolites sharing 32 common CRC targets. Protein-protein interaction and pathway enrichment analyses identified hub genes including EGFR, PIK3CA, PIK3CB, KDR, ESR1, AR, and MET with enrichment in the PI3K-Akt signaling pathway, suggesting mechanisms related to oxidative stress, apoptosis, and tumor cell proliferation.

These predictions were validated using MTT assays at 24, 48, and 72 h against HCT116 and HT29 CRC cell lines and non-cancerous HaCaT keratinocytes. Several cultivars exhibited cytotoxicity towards CRC cells in a time- and dose-dependent manner, while demonstrating lower toxicity towards HaCaT cells. One pigmented accession emerged as the most promising candidate, with a 72-hour IC_{50} of 117.18 µg/mL against HCT116 cells and exceeding 1000 µg/mL in HaCaT cells, resulting in a selectivity index above 8.5.

Collectively, these findings provide experimental and systems-level evidence supporting the Rasāyana relevance of indigenous pigmented rice bran and underscore their potential as sources of chemopreventive metabolites targeting PI3K–Akt-associated CRC pathways. This integration establishes a foundation for discovering functional food-derived anti-cancer bioactives.



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Sciforum-195852: Serum short-chain fatty acids: associations with diet and insomnia occurrence in peri- and postmenopausal women. Preliminary cross-sectional study

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Introduction: The short-chain fatty acids (SCFAs) are important mediators of the gut-brain axis and can influence the regulation of circadian rhythms. The study aimed to evaluate the associations between serum concentrations of SCFAs with food consumption and insomnia occurrence among peri- and postmenopausal women.

Methods: This preliminary cross-sectional study involved 82 women aged 50-70 from north-eastern Poland. The occurrence of insomnia was diagnosed in 38 women, using the Women's Health Initiative Insomnia Rating Scale. Dietary data were collected with a food frequency questionnaire (62-item FFQ-6®). The serum concentrations of six SCFAs (acetic, propionic, butyric, isovaleric, valeric, isobutyric) were analysed using the GC-MS technique.

Results: Women who ate sweets at least once a day had lower serum concentrations of acetic (316.9 vs. 389.4 μmol/l;p=0.0161) and propionic acids (18.9 vs. 20.9 μmol/l;p=0.0490) compared to women who ate these products less frequently. Similarly, eating fats such as margarine or mayonnaise at least several times a week or alcoholic beverages at least once a month was associated with lower concentrations of valeric (2.1 vs. 2.6;p=0.0105) or isovaleric acids (6.9 vs. 7.9 μmol/l;p=0.0458), respectively. In turn, eating cheese or eggs at least several times/week was associated with higher concentrations of acetic (378.1 vs. 348.4 μmol/l;p=0.0344) and isovaleric acids (7.8 vs. 6.6 μmol/l;p=0.0251) or propionic acid (20.8 vs. 17.7 μmol/l;p=0.0400), respectively. There was no significant difference in SCFAs concentrations in association with the occurrence of insomnia.

Conclusions: The obtained results indicate a positive association between the moderate consumption of cheese and eggs and the synthesis of selected SCFAs. In turn, consumption of sweets, alcohol and highly processed fats was inversely associated with serum levels of SCFAs. No significant associations were found between SCFAs and insomnia. Due to the limitations of SCFAs analyses in serum only and the collection of qualitative dietary data, to confirm these findings, a prospective study involving microbiome analysis is needed.



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Sciforum-196013: Personal Urinary Metabotypes and Sex Differences Dominate Seasonal and Dietary Effects in a Four-Season Longitudinal Urine Metabolomics Study

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Urinary metabolomics captures integrated information on host physiology, diet, and microbial co-metabolism. However, the relative contribution of stable biological traits, seasonal variation, and short-term dietary perturbations remains difficult to disentangle. This study aimed to define the hierarchy of factors shaping urinary metabolomic variability in a longitudinal four-season dietary intervention.

A total of 93 urine samples from eight healthy participants were collected across four seasons before and after a short-term controlled dietary intervention. The final dataset comprised 827 metabolomic features (levels 1–3 annotations) and nine clinical urinary variables. Global variance partitioning was assessed using single-factor PERMANOVA, while Principal Component Analysis (PCA) and cross-validated Partial Least Squares Discriminant Analysis (PLS-DA) with permutation testing were used to evaluate group separation and classification performance.

Participant identity was the dominant source of metabolomic variation, explaining 36.5% of the total variance ($p = 0.005$). Sex emerged as the second most important factor, accounting for 9.0% of the variance. PCA revealed clear separation between male and female samples, and PLS-DA further supported strong sex-related metabolic differences (balanced accuracy = 1.00; permutation $p = 0$). In contrast, season explained only 4.6% of the variance ($p = 0.03$), while dietary phase and pre/post-intervention status accounted for 2.6% and 1.2%, respectively, with limited evidence of global clustering. Repeated samples from the same participant were consistently more similar than samples from different individuals, supporting the existence of stable personal urinary metabotypes.

These findings indicate that individual metabolic signatures and sex-specific differences are the primary determinants of urinary metabolomic structure, whereas seasonal and dietary influences produce comparatively modest within-individual shifts. The results highlight the importance of incorporating both subject identity and sex into the design and interpretation of nutritional metabolomics studies.



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Sciforum-196056: "The testis remembers": lifestyle-based weight loss partially rescues fertility despite testicular metabolic memory of early-life obesity

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Childhood obesity is a risk factor for male infertility, creating the need for non-pharmacological therapeutic strategies. Thus, we aimed to assess whether lifestyle-based strategies mitigate the negative metabolic and reproductive effects of early-life obesity. We developed a *Mus musculus* model, divided into five cohorts: control (CTRL), control diet and baseline activity (200 days); diet-induced obesity (DIO), lifelong high-fat diet (HFD) and baseline activity (200 days); DIO with dietary correction (DIOc), HFD (60 days) followed by a switch to control diet (140 days); DIO with aerobic exercise (DIO_EX), lifelong HFD (200 days), treadmill exercise during the final 140 days; DIO with dietary correction and aerobic exercise (DIOc_EX), HFD (60 days) followed by a switch to control diet and treadmill exercise (140 days). Body and organ weight were recorded. Intraperitoneal glucose and insulin tolerance tests (ipGTT and ipITT) were performed. Estradiol (E_2) and testosterone (T) were measured through ELISA. Hematoxylin-eosin-stained sections were examined for testicular histological characterization. Testicular metabolomes were characterized through untargeted ^{1}H-NMR metabolomics. DIO established a phenotype of metabolic syndrome (glucose intolerance) and reproductive decline (elevated E_2/T and poor sperm quality). While all interventions normalized the E_2/T ratios, diet-based interventions (DIOc and DIOc_EX) were superior in reducing weight, restoring glucose homeostasis, and testicular histoarchitecture. Sperm parameters showed the greatest rescue in the exercise-based groups (DIO_EX and DIOc_EX). Metabolomic profiling revealed a "testicular metabolic memory", characterized by a depletion of energy and antioxidant metabolites that persisted despite weight loss. Our data demonstrates that functional reproductive recovery can occur despite the altered testicular metabolome, suggesting that sperm quality may improve without complete metabolic recovery. Our results also support a "Two-Hit" recovery model, in which diet improves systemic damage and exercise improves sperm quality. This establishes multimodal lifestyle-based therapies as a mechanistically superior framework for addressing obesity-related subfertility.



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Sciforum-196092: The EV–Oxylipin Axis in Atherosclerosis: Characterization of oxylipin cargo in plasma-derived extracellular vesicles from *Ldlr*$^{-/-}$ mice

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Atherosclerosis is a chronic inflammatory disease driven by dysregulated lipid metabolism and immune activation. Extracellular vesicles (EVs) have emerged as important mediators of intercellular communication in cardiovascular disease, capable of transferring bioactive cargo including lipids. Oxylipins are bioactive oxidized metabolites of polyunsaturated fatty acids regulate inflammation, vascular tone, and immune activation. Despite growing interest in both EVs and oxylipins, the oxylipin cargo of circulating EVs and how it is remodeled under atherogenic conditions remain poorly understood. To characterize the oxylipin composition of plasma-derived EV subpopulations from *Ldlr*$^{-/-}$ mice and determine how atherogenic dietary conditions alter the EV–oxylipin profile.

Plasma from *Ldlr*$^{-/-}$ mice fed a Western diet (WD) or control diet (CD) was fractionated by size exclusion chromatography into an LDL-enriched fraction (F0) and two EV-enriched fractions (F1, F2). EV isolation was confirmed by nanoparticle tracking analysis (NTA). Oxylipins were quantified by targeted mass spectrometry and normalized to total protein.

NTA showed WD mice produced EVs with higher concentrations and larger particle sizes, particularly in F1 (~30 × 10^6 vs ~12 × 10^6 particles/mL; ~141 vs ~117 nm). We detected 72 oxylipin species across eight fatty acid precursors, dominated by arachidonic acid (AA, n=33), followed by LA (n=11), EPA (n=11), DHA (n=9), ALA, DHGLA, GLA, and mead acid. AA-derived pro-inflammatory mediators including HETEs, KETEs, DiHETrEs, and prostanoids (PGD2, PGE2, PGF2α, 6-keto-PGF1α) were broadly upregulated in WD fractions. CD fractions showed enrichment of EPA-derived HEPEs and DHA-derived HDoHEs, including the pro-resolving mediator RvD2. In the EV1 fraction, 16 oxylipins were detected exclusively under WD nearly three times the 6 oxylipins unique to CD suggesting broader activation of AA-dependent enzymatic pathways under atherogenic stress.

These findings reveal a diet-driven remodeling of the EV–oxylipin axis in *Ldlr*$^{-/-}$ mice, shifting from a pro-resolving signature under CD toward a pro-inflammatory eicosanoid-enriched profile under WD, implicating EV-associated oxylipins in vascular inflammation during atherogenesis.



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Sciforum-196093: Metabolite Profiling of Selected Mauritian Endemic Fruits

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Endemic plants' fruits contain flesh and seeds that are metabolically dense organs storing concentrated bioactive compounds, yet they remain frequently overlooked in phytochemical research. Mauritian endemic plants represent a unique reservoir of biodiversity with significant potential for the discovery of bioactive compounds. Among these, *Tambourissa ficus* (Monimiaceae), *Diospyros tessellaria* (Ebenaceae), and *Sideroxylon cinereum* (Sapotaceae) produce edible fruits consumed by humans and local fauna without reported adverse effects. However, the phytochemical composition of these fruits remains largely unexplored. The current study aims at identifying volatile compounds of the methanolic seed extracts using gas chromatography–mass spectrometry (GC–MS) and evaluating the cytotoxicity of these extracts in HGL5 ovarian cell lines using the Alamar Blue cell viability assay. ANOVA was performed followed by Dunnett's post hoc test using GraphPad Prism (GraphPad Software, CA, USA). The results were reported as the mean standard deviation of three analytical triplicates with significance set at $p \leq 0.05$. GC–MS analysis of each extracts identified 15 phytochemical constituents. The predominant compounds in the fruits flesh were β-sitosterol (44.33%), 1,4-naphthoquinone, 6-ethyl-2,5-dihydroxy- (51.18%), and lanosta-8,24-dien-3-ol acetate (52.11%). Other notable constituents included β-chamigrene, plumbagin, stigmasterol, γ-sitosterol, oleanenyl acetate, friedelane, and dammaradienyl acetate. Overall, the fruit flesh exhibited a diverse phytochemical profile dominated by sterols, quinones, terpenoids, and triterpenoids, suggesting potential bioactive properties. These compounds have diverse potential for medicinal, nutritional, and cosmetic applications. No statistically significant reduction in cell viability was observed ($p > 0.05$), indicating a favourable safety profile. The rich profile of triterpenoids and phytosterols, highlights the potential of Mauritian fruits as sources of pharmacologically active compounds rather than solely nutritional lipids.



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Sciforum-201320: Astaxanthin Supplementation Mitigates Chronic Heat Stress-Induced Dysregulation of Glycerophospholipids and Sphingolipids in Broiler Thigh Muscle: Untargeted LC-MS Lipidomics Evidence

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Chronic heat stress induces oxidative damage and lipid metabolic disruption in broiler skeletal muscle, yet its molecular effects on glycerophospholipids and sphingolipids remain poorly characterised. This study investigated the lipidomic effects of chronic heat stress and dietary astaxanthin (AST) supplementation (40 mg/kg) on broiler thigh muscle using untargeted liquid chromatography–mass spectrometry. Three experimental groups were established in this study, including a thermoneutral control group (Group A), a chronic HS group (Group B; 34 °C, 8 h/day), and an HS group supplemented with dietary AST (Group D). Orthogonal partial least squares discriminant analysis (OPLS-DA) revealed robust group discrimination ($R^2Y \geq 0.987$, $Q^2Y \geq 0.784$), with 301 differentially expressed lipid species identified (VIP ≥ 1 and $P < 0.05$.). HS significantly depleted polyunsaturated phosphatidylethanolamine species such as PE(54:3), PE(58:5), LPE(18:2), and LPE(22:5) and markedly reduced PI(42:0), indicating oxidative membrane phospholipid degradation. Concurrently, sphingolipid dysregulation was evidenced by pronounced accumulation of Hex1Cer(d18:2_22:5), sphingoid bases SPH(d15:1) and SPH(d16:1), and GM3 gangliosides, reflecting pro-inflammatory ceramide signalling. AST supplementation effectively reversed these disturbances, restoring glycerophospholipid abundance, suppressing ceramide accumulation, and normalising sphingoid base levels. KEGG pathway enrichment identified glycerophospholipid metabolism as the primary disrupted pathway. These findings demonstrate that AST serves as a potent nutritional intervention to stabilize the thigh muscle lipidome of broilers under chronic heat stress, offering new insights into maintaining muscle lipid quality in thermally challenged poultry farming.



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Sciforum-203067: Nutrient-Dense Wheatgrass Ladoo Formulations for Athlete Nutrition: A Biochemical Profiling of Sunflower and Pumpkin Seed Variants

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Nutrition-focused metabolite and food composition analyses are increasingly relevant for designing functional foods for athletic populations. This study developed nutrient-dense wheatgrass ladoo formulations enriched with sunflower seeds and pumpkin seeds, evaluating their nutritional and physicochemical characteristics as potential snack options for athletes. Ingredients were procured from licensed vendors and processed through roasting, grinding, mixing, and shaping. Samples were analyzed at the FICCI laboratory, with sensory evaluation by 25 semi-trained panelists assessing appearance, taste, color, texture, aroma, sweetness, and overall acceptability; pH analysis compared the two variants.

Nutritional analysis showed the sunflower seed variant contained 45.53 g carbohydrates, 26.3 g protein, and 21.76 g fat per 100 g, while the pumpkin seed variant contained 54.4 g carbohydrates, 32.7 g protein, and 24 g fat per 100 g, indicating notable variation in nutrient density. A statistically significant mean difference of 0.29889 pH units was observed between variants ($p < 0.001$), suggesting formulation-dependent differences potentially influencing stability and sensory quality.

This study did not include micronutrient or bioactive phytochemical profiling; however, published literature indicates sunflower seeds contain tocopherols, phenolic acids (chlorogenic, caffeic, ferulic, gallic, protocatechuic, coumaric, sinapic acids), flavonoids (quercetin, kaempferol, luteolin, apigenin, heliannone), carotenoids, L-ascorbic acid, and antioxidant enzymes; pumpkin seeds contain phytosterols (β-sitosterol), tocopherols, carotenoids (lutein, zeaxanthin), phenolic compounds (vanillic, ferulic, tyrosol, luteolin, sinapic acids, trigonelline, D-chiro-inositol, nicotinic acid), cucurbitacins, lignans, and selenium; wheatgrass contains flavonoids (rutin, quercetin), phenolic acids (gallic acid), vitamins, minerals, and proteins. These compounds are associated with antioxidant capacity, metabolic health, exercise recovery, and athlete health in published literature, and their absence in this characterization represents a limitation warranting future investigation.

Wheatgrass ladoos enriched with sunflower and pumpkin seeds may serve as practical, natural, nutrient-rich snack alternatives for athletes, supporting functional food development aligned with sports nutrition



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Sciforum-204584: LC-MS-Based Metabolomic Characterization of an Unsaponifiable *Bixa orellana* Fraction Before and After Tocotrienol Enrichment

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The industrial processing of *Bixa orellana* L. seeds for bixin production generates large amounts of lipid-rich residues with potential as sources of bioactive compounds. These by-products contain tocotrienols and other lipophilic metabolites with antioxidant, anti-inflammatory, and antiproliferative properties. Untargeted metabolomics is a valuable strategy for characterizing these complex matrices and supporting their valorization within circular economy approaches. This study compared the metabolomic profiles of two fractions obtained from industrial processing: TT, the unsaponifiable residual fraction from bixin production, and T3, a tocotrienol-enriched fraction produced from TT by molecular distillation. Samples (10 mg/mL) were dissolved in hexane, diluted in methanol, and analyzed in triplicate by UPLC-QTOF-MS using MSE acquisition in positive and negative electrospray ionization modes (m/z 100–1000). Data were processed in Progenesis™ QI v2.4 and analyzed in MetaboAnalyst 5.0 after sum normalization, log transformation, and Pareto scaling. Differential features were selected using fold change ≥2.0 and FDR-adjusted $p < 0.05$. Initially, 2444 positive-mode and 1578 negative-mode features were detected. After quality filtering (RSD <25%), 1677 and 864 features remained, respectively. Comparative analysis identified 453 differential features in positive mode and 163 in negative mode. Principal Component Analysis showed clear metabolic discrimination between TT and T3, demonstrating that molecular distillation substantially altered the metabolomic composition of the original residue. Putative annotation indicated enrichment of fatty acids and derivatives, sesquiterpenes, diterpenes, carotenoids/apocarotenoids, sphingolipids, and complex lipids in T3, whereas TT showed higher abundance of terpenoids, oxylipins, phospholipids, steroids/sterols, lipophilic phenolics, and nitrogen-containing lipids. Overall, 79 differential features were plausibly annotated. These findings demonstrate that molecular distillation selectively enriches tocotrienol-associated metabolites and highlight the biotechnological and pharmaceutical potential of *B. orellana* industrial by-products, supporting untargeted LC-MS metabolomics as a powerful tool for their characterization and valorization.



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Sciforum-205906: NUTRACEUTICAL EFFECT OF AÇAÍ ON SPERM FUNCTION IN THE D-GALACTOSE-INDUCED AGING MODEL IS NOT LINKED WITH GLYCOLYSIS PATHWAY METABOLOMICS

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Açaí (*Euterpe olaracea Mart.*) is a Brazilian "super" fruit rich in polyphenols with antioxidant and anti-inflammatory properties. Aging is associated with increased oxidative stress and chronic low-grade inflammation—impairing the male reproductive system. Overconsumption of D-galactose (DG) reproduces some of the hallmarks of aging, including oxidative damage, DNA damage, and innate immune system and circulatory dysregulation. Therefore, this preliminary study aimed to evaluate whether freeze-dried açaí supplementation attenuates metabolic alterations and reproductive dysfunction in a rat model of accelerated aging.

Twenty-four male Wistar rats (8 weeks old) were randomly distributed into four experimental groups (*n=6*/group): Control, DG (200 mg/kg/day), Açaí (300 mg/kg/day), and DG + Açaí (DGA). After four weeks of voluntary consumption, sperm concentration, motility, and morphology were evaluated. Urinary metabolomic (pyruvate, lactate, citrate, acetone, succinate, hippurate) was assessed through proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy. Data were analyzed using parametric and non-parametric ANOVA tests, and Spearman's correlation matrix, with significance set at $p < 0.05$.

Metabolomic analysis revealed no significant differences in urinary metabolics (*Kruskal–Wallis,* $p > 0.05$). Descriptively, the highest mean normalized glycine and lactate levels were observed in the DG group, while the lowest mean normalized pyruvate level was observed in the DGA group. Spearman correlation analysis did not demonstrate significant associations between metabolites and sperm motility. As expected, positive correlations were observed among pyruvate, succinate, citrate, glycine, lactate, and acetone.

Our results indicate that the coordinated pattern observed among metabolites supports coherent metabolic changes during the initial stage of reproductive dysfunction. Metabolites involved in glycolysis analysed by RMN neither mirrored the energetic dysfunction caused by D-galactose-induced aging in a short protocol nor the biological benefits of açaí seen in sperm function. Further studies should address whether longer exposure to D-galactose and more sensitive techniques would reveal metabolic modulation provided by açaí.



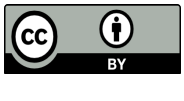
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Sciforum-206939: Lipidomic Profiling of Egg Yolk to Evaluate Alternative Protein Sources in the Mediterranean Diet

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Alternative protein sources, such as plant-based, microbial and novel foods, offer promising solutions to meet the growing population's nutritional needs while reducing environmental impact. The ProxIMed project aims to integrate sustainable proteins into Mediterranean food systems. Eggs from hens (6 groups, 6 replicates per group) were collected after 21 and 42 days of feeding intervention with the basal diet supplemented with 10% of one of the following feed materials: sesame hulls, date seeds, fava beans, Tenebrio molitor larvae, or hydrolyzed Hermetia illucens. All experimental diets were designed to be isoenergetic and isoproteic, ensuring comparable levels of metabolizable energy (approximately 11.4 MJ/kg) and crude protein (17.5%) across all treatments. Different extraction solvents (MTBE, chloroform, MeOH and H2O) in different ratios were evaluated for lipid extraction. After optimization, frozen and lyophilized egg yolks were compared to assess their lipidomic content. The optimal extraction condition was MTBE:MeOH:H_2O 2:1:1 (v/v/v). Comparative analysis revealed that frozen samples yielded higher lipid coverage and signal intensity. A total of 72 frozen egg yolk samples were analyzed using a UHPLC-timsTOF Pro 2 analytical platform in PASEF mode, allowing high-throughput profiling and lipid annotation using collision cross section (CCS) measurements. Lipid identification was performed using PASEF fragmentation data and available lipid libraries (MS-DIAL, LIPID ATLAS, and an in-house NIST database). Almost 400 lipids were identified, covering major lipid subclasses, including CE, CER, DG, HexCer, PE, PE-O/PE-P, PC-O/PC-P, LPC, LPE, PI, SM, PC, TG and FA. Multivariate analysis revealed diet-related differences in egg yolk lipidomic profiles, particularly among control, fava bean, Tenebrio molitor and hydrolyzed Hermetia illucens groups. These findings demonstrate the potential of lipidomics to evaluate the effects of alternative protein ingredients on egg yolk lipid composition.



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Sciforum-207022: Why Some Individuals Gain Weight While Others Do Not: Integrating Metabolomics and Nutrigenomics for Precision Weight Management

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Body weight regulation is governed by complex interactions among genetic predisposition, metabolic efficiency, nutrient sensing, gut microbial metabolism, and environmental exposures rather than caloric intake alone. Considerable inter-individual variability explains why some individuals remain lean despite high energy consumption, whereas others develop obesity despite consuming relatively modest amounts of food. Studies estimate that 40-70% of BMI variability is heritable, highlighting a substantial genetic contribution to body weight regulation. The largest genome-wide association study, including 681,275 individuals, identified more than 900 genomic loci associated with BMI and adiposity, implicating genes involved in appetite regulation, adipogenesis, insulin signaling, and energy expenditure, including FTO, MC4R, TMEM18, SH2B1, LEPR, BDNF, PPARG, and ADCY3. Individuals carrying two copies of the FTO risk allele have approximately 1.67-fold higher odds of obesity and weigh 3-4 kg more than non-carriers. Prospective cohort studies show that circulating branched-chain amino acids, aromatic amino acids, acylcarnitines, ceramides, and altered bile acids are elevated years before the onset of insulin resistance and type-2 diabetes. Individuals in the highest quartile of plasma BCAA concentrations exhibit approximately a two-fold greater risk of developing type 2 diabetes, independent of BMI. Lipidomic analyses have additionally identified ceramides as predictors of adipose tissue dysfunction, chronic inflammation, and cardiometabolic risk. Emerging evidence also indicates that gut microbiota-derived metabolites, including short-chain fatty acids, secondary bile acids, trimethylamine-N-oxide, and indole derivatives, regulate host energy harvest, mitochondrial β-oxidation, and inflammatory pathways, contributing to differential weight trajectories. Variants in FTO, PPARG, APOA2, TCF7L2, and ADRB2 influence satiety, lipid oxidation, glucose metabolism, and weight-loss responsiveness, explaining why identical dietary regimens produce markedly different outcomes among individuals. Integrating genomics, metabolomics, microbiome profiling, and clinical phenotyping enables precision nutrition approaches capable of identifying metabolic responders and tailoring individualized dietary prescriptions. Such multi-omics strategies represent a paradigm shift from conventional calorie-restriction models toward mechanism-based weight management.



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Sciforum-207117: Annona muricata Leaf Extract Improves Metabolic Biomarkers and Tissue-Specific Lipid Metabolism in Diet-Induced Obese Mice

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Introduction

Altered lipid metabolism drives obesity-associated metabolic dysfunction and hepatic steatosis. Although *Annona muricata* has shown promising metabolic effects, the molecular mechanisms underlying these effects remain unclear. This study evaluated the effects of *A. muricata* leaf extract on metabolic biomarkers and tissue-specific changes related to lipid metabolism in diet-induced obese mice.

Methods

Male BALB/c mice (n = 42) were randomly allocated to six experimental groups: normal diet (ND), high-fat diet (HFD), HFD supplemented with *Annona muricata* leaf extract (250 or 500 mg/kg; HFD-AM250 and HFD-AM500), HFD plus metformin (HFD-MET), and a transition group (TRANS). Obesity was induced by HFD feeding for 8 weeks followed by 6 weeks of treatment. Serum glucose, triglycerides, HDL-cholesterol, ALT, AST, and hepatic steatosis were evaluated. Relative expression of *Ampk, Pparα, Pparγ, Srebf1,* and *Fasn* was determined in liver, whereas *Ampk, Pparγ, C/ebpα,* and *Fabp4* were analyzed in adipose tissue by RT-qPCR. Data were analyzed using ANOVA or Kruskal–Wallis tests.

Results

Compared with untreated HFD mice, *Annona muricata* leaf extract (500 mg/kg) significantly improved metabolic biomarkers by reducing serum glucose, triglycerides, ALT and AST activities while increasing HDL-cholesterol (all $p < 0.05$). Treatment also markedly attenuated hepatic steatosis (6.3 ± 2.3% vs. 21.1 ± 3.1% in HFD mice). In the liver, the extract increased *Ampk* and *Pparα* expression while decreasing *Pparγ, Srebf1,* and *Fasn*. In adipose tissue, treatment increased *Ampk* expression and decreased *Pparγ, C/ebpα,* and *Fabp4* expression (all $p < 0.05$).

Conclusions

Annona muricata leaf extract improved metabolic biomarkers and attenuated hepatic steatosis, accompanied by tissue-specific changes associated with lipid metabolism in the liver and adipose tissue. These findings suggest that A. muricata leaf extract has potential as a bioactive nutritional intervention for improving obesity-associated metabolic dysfunction.



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Sciforum-207236: Dietary Grape Pomace Polyphenols Modulate Hepatic Fatty Acid Metabolism in Early Diet-Induced MASLD

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Alterations in hepatic fatty acid synthesis and oxidation contribute to lipid accumulation during the early stages of metabolic dysfunction-associated steatotic liver disease (MASLD). Dietary polyphenols have attracted attention because of their potential to regulate these metabolic pathways. Grape pomace, a by-product of the wine industry, is particularly rich in polyphenols. This study investigated the effects of grape pomace extract (GPE) supplementation on hepatic lipid metabolism in rats fed a high-fat, high-fructose (HFHF) diet.

Male Wistar rats were assigned to four groups (final n = 5–6/group; one HFHF rat was lost during the study) and fed for 9 weeks with either a control diet, a control diet supplemented with 2% GPE, an HFHF diet, or an HFHF diet supplemented with 2% GPE. Body and liver parameters were recorded, liver histology was evaluated using the NAFLD Activity Score (NAS) and Hepatic Activity Index (HAI), and immunohistochemistry was used to assess phosphorylated acetyl-CoA carboxylase (pACC Ser79), carnitine palmitoyltransferase 1 (CPT1), phosphorylated NF-κB (pNF-κB), and nitrotyrosine. Since histological scores were ordinal, statistical analyses were performed using the Kruskal–Wallis test.

HFHF-fed rats exhibited increased body weight and moderate macro- and microvesicular steatosis, consistent with early MASLD. GPE supplementation was associated with a lower NAS (1.67 ± 1.03 vs. 3.20 ± 0.45), absence of hepatocyte ballooning, and reduced steatosis, although the NAS reduction was not statistically significant. GPE partially restored pACC levels and significantly increased CPT1 expression compared with the unsupplemented HFHF group ($p < 0.05$). Cytoplasmic pNF-κB levels were reduced after GPE supplementation, whereas nitrotyrosine levels remained unchanged.

These findings indicate that GPE attenuated early hepatic steatosis and modulated key markers of hepatic lipid metabolism in HFHF-fed rats. The observed changes in pACC and CPT1 support the potential of grape pomace polyphenols as a nutritional strategy for early MASLD. Future studies should compare GPE with established pharmacological therapies to better contextualize its therapeutic efficacy for MASLD prevention.



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Sciforum-207308: Tumbo Seed Oil Modulates Lipid Metabolism in Experimental Diet-Induced Hyperlipidemia

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Background: Tumbo (*Passiflora tripartita* var. *mollissima*) is an Andean fruit whose seeds are commonly discarded as agro-industrial by-products, despite their potential as a source of bioactive lipids and antioxidant compounds. Their valorization could contribute to the development of functional ingredients with relevance to lipid and nutrition metabolism. **Objective:** To characterize tumbo seed oil and evaluate its effect on serum lipid metabolism in an experimental model of diet-induced hyperlipidemia. **Methods:** The oil was obtained by mechanical pressing at 60 °C. Acidity, peroxide, and iodine values were determined according to AOCS methods. Fatty acid composition was analyzed by gas chromatography. Antioxidant capacity was evaluated using ABTS, DPPH, and FRAP assays, while total phenolic and flavonoid contents were determined using the Folin–Ciocalteu and aluminum chloride methods, respectively. Guinea pigs were distributed into four groups: healthy control, hyperlipidemic control, olive oil treatment, and tumbo seed oil treatment. At the end of the experimental period, serum total cholesterol, triglycerides, HDL-c, LDL-c, and VLDL-c were determined. Data were analyzed using the Kruskal–Wallis test followed by Dunn's post hoc test. **Results:** The oil showed low acidity, low peroxide value, and high iodine value, suggesting good initial quality and a high degree of unsaturation. Linoleic acid was the predominant fatty acid, followed by oleic, palmitic, and stearic acids. The oil also showed relevant antioxidant capacity in the evaluated assays. The hyperlipidemic group showed increased total cholesterol, triglycerides, and VLDL-c compared with the healthy control group. Tumbo seed oil treatment reduced total cholesterol, triglycerides, LDL-c, and VLDL-c, while increasing HDL-c compared with the hyperlipidemic control group. **Conclusions:** Tumbo seed oil showed a highly unsaturated lipid profile, relevant antioxidant capacity, and potential to modulate serum lipid metabolism in experimental hyperlipidemia, supporting its interest as a bioactive ingredient in lipid and nutrition metabolomics research.



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Sciforum-207314: A comparative analysis of different lipidomics workflow for optimized identification and quantitation

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Lipidomics analysis involves processing lipid species from complex biological matrices. There are several approaches available to perform lipidomics analysis. Mass-spectrometry based lipidomics analysis is one of the powerful tools to perform both untargeted and targeted lipidomics. Although high-resolution mass spectrometry is well-suited for the robust profiling and relative quantification of the lipidome, the success of lipidomics analysis relies heavily on post-acquisition factors, particularly the data processing tools and workflows. There are several algorithms and software are developed to analyze lipid species. However, the optimized workflow is still underway. In this study, we have compared three different lipidomics workflows to evaluate the accurate identification and quantitation of lipids from complex NIST plasma. Lipids from NIST plasma sample were extracted using acidified CHCl3/MeOH method with addition of Equisplash (Avanti) internal standard. Extracted lipids were separated by RP-UHPLC and analyzed in both ESI+/ESI-mode using a high-resolution Exploris480 MS (Thermo) operated in DDA mode. Raw data were processed using MS-Dial v5.5, Compound Discoverer v3.5 and LipidSearch 5.1. Data analysis was performed using in house R script. Our preliminary results exhibited 31,140 features from more than 80% of the samples with RSD less than 30%. The curated datasets, include only MS/MS-annotated lipids, were used for further comparison. Comparative analysis of untargeted data revealed that over ~93% data shared similarity across all three different platforms. The most common lipid classes are PC, PE, PI, TG, DG, and CE. While lipidomics software showed similar class coverage, performance varied slightly when identifying isobaric lipids across different platforms. Analysis of the curated datasets yielded 1,670 (Compound Discoverer), 1,663 (MS-DIAL), and 1,522 (LipidSearch) lipid species. Although MS-Dial is a free, comprehensive tool for broad lipidomic summaries, paid platforms such as LipidSearch and Compound Discoverer provides deeper, specialized insights into specific lipids such as acyl-CoAs and carnitines.



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Session 2. Ecological and Environmental Metabolomics

Sciforum-184632: Using metabolomic tools to bioprospect the antibacterial activity of a seaweed endophyte co-cultured with biofilm-forming bacteria *Pseudomonas aeruginosa*

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The increasing prevalence of bacterial biofilms and their tolerance to antimicrobial treatment highlight the need for new anti-biofilm agents. Microbial co-culture offers a promising strategy for inducing otherwise poorly expressed secondary metabolites; however, the metabolic responses to fungal–bacterial interactions and their contribution to antimicrobial activity remain insufficiently understood. This study investigated whether co-culturing the algal endophytic fungus *Dendryphiella salina* with the biofilm-forming bacterium *Pseudomonas aeruginosa* could induce bioactive metabolites with anti-biofilm activity.

An integrated workflow combining multivariate data analysis, Nuclear Magnetic Resonance (NMR) spectroscopy, High-Performance Liquid Chromatography–High-Resolution Mass Spectrometry (HPLC–HRMS), and antimicrobial and anti-biofilm assays was used to characterise co-culture-induced metabolic changes and identify bioactive metabolites. Optimised co-culture conditions were selected based on metabolic profiles and biological activity and subsequently scaled up for chemical investigation. Medium-pressure liquid chromatography fractionation of the crude extract generated fourteen fractions, nine of which exhibited significant anti-biofilm activity against methicillin-resistant *Staphylococcus aureus* (MRSA). OPLS-DA, HRMS-based dereplication, and 1D/2D NMR spectroscopy enabled the annotation of several metabolites, including linoleic acid, 2-(2-hydroxyphenyl)thiazole, 2-phenyl-4,5-dihydrothiazol-4-ol, aeruginoic acid, dihydroaeruginoic acid, and a mono-rhamnolipid.

The mono-rhamnolipid demonstrated the strongest overall activity, with a minimum inhibitory concentration (MIC) of 6.5 µg/mL, minimum biofilm prevention concentration (MBPC) of 5.0 µg/mL, and minimum biofilm inhibitory concentration (MBIC) of 7.2 µg/mL. A mixture of 2-phenyl-4,5-dihydrothiazol-4-ol and dihydroaeruginoic acid inhibited planktonic growth, biofilm formation, and established biofilms by 95.3%, 98.9%, and 85.1%, respectively. Overall, fungal–bacterial co-culture induced substantial metabolic and biological changes and facilitated the discovery of anti-MRSA metabolites. Notably, anti-biofilm activity was predominantly associated with bacterial secondary metabolites, suggesting that microbial interactions can redirect secondary metabolism towards bioactive compounds.



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Sciforum-189779: Co-Culture-Induced Antibacterial Metabolites from Seaweed Endophytes: A Metabolomics Approach

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This study aimed to identify antimicrobial secondary metabolites produced through the co-cultivation of the algal endophytic fungi *Dendryphiella salina* and *Coprinellus micaceus*, isolated from the Scottish seaweeds *Laminaria hyperborea* and *Fucus vesiculosus*, respectively. An integrated analytical approach combining multivariate data analysis, Nuclear Magnetic Resonance (NMR) spectroscopy, High-Performance Liquid Chromatography coupled with High-Resolution Mass Spectrometry (HPLC–HRMS), and anti-biofilm assays was employed to screen and optimise co-culture conditions for large-scale cultivation. These techniques enabled the systematic evaluation of metabolomic changes induced by fungal interaction and the selection of conditions that enhanced antibacterial activity.

To identify antibacterial compounds present in the crude co-culture extract, fractionation was performed using medium-pressure liquid chromatography (MPLC) to purify the bioactive metabolites further. Thin-layer chromatography resolved sixteen fractions with distinct chemical profiles, of which ten exhibited significant antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA). Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA), combined with HRMS-based dereplication and supported by 1D and 2D NMR analyses, facilitated the annotation of several metabolites, including α-linoleic acid, orsellinaldehyde, orsellinic acid, orcinol, α-acetylorcinol, p-salicylic acid, 4-hydroxyphenylacetone, and caffeic acid.

Orsellinic acid, orcinol and 2,5-dihydroxy-3-(hydroxymethyl)benzoic acid were detected in the *D. salina* monoculture, whereas co-cultivation resulted in significant alterations in the metabolite profile of both fungi, indicating that interspecies interactions stimulated the production of additional secondary metabolites and enhanced antibacterial activity. These findings demonstrate the potential of co-culture-based metabolomic strategies for the discovery of bioactive natural products from marine-derived fungi.



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Sciforum-194583: Metabolite identification of alpha-cypermethrin biodegradation by citrus bacteria.

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Alpha-cypermethrin is a type II pyrethroid insecticide widely used in agriculture, including for citrus production, but its persistence and toxicity to non-target organisms raise environmental and health concerns. In this study, citrus-associated bacteria were evaluated for the biodegradation of (±)-alpha-cypermethrin, with emphasis on metabolite identification and pathway elucidation. *Priestia megaterium* CBMAI 2842 isolated from orange leaves, were cultivated in liquid medium containing 100 mg L^{-1} of commercial (±)-alpha-cypermethrin and incubated at 32 °C and 130 rpm for 5 days. Metabolites were investigated by GC–MS and LC–MS/MS-based untargeted metabolomics. LC-MS/MS-based revealed a clear metabolic differentiation between biodegradation samples and control groups, supporting the formation of biodegradation-related features and confirming that α-cypermethrin transformation by *P. megaterium* CBMAI 2842 induces a distinct metabolic profile. The tentatively identified compounds by LC-MS/MS were 3-phenoxybenzoic acid, hydroxy-3-phenoxybenzoic acid, permethrinic acid, 3-phenoxybenzamide, a ketone derivative and 3-phenoxybenzaldehyde. GC–MS analysis enabled the tentatively identification of ten metabolites associated with alpha-cypermethrin transformation. The detected metabolites suggest that biodegradation occurs mainly through ester bond hydrolysis, followed by oxidation, reduction, ether bond cleavage, and formation of lower-molecular-weight aromatic compounds. These findings indicate that P. megaterium CBMAI 2842 is an efficient citrus-associated biocatalyst for alpha-cypermethrin transformation and may contribute to future bioremediation strategies for pyrethroid-contaminated environments.



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Sciforum-206079: Comparative Analysis of Sample Preservation Techniques for Plant Ecometabolomic Studies

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Metabolomics holds great potential for ecological studies, as a sensitive technique that generates extensive, complex datasets about the metabolic state of target species. A major challenge in achieving standardized results lies in sample collection and storage, particularly regarding biological material found in remote locations, far from research facilities. In such contexts, onsite sample preservation using liquid nitrogen or solvents can become unfeasible. Therefore, this study aimed to compare two preservation methods for plant samples, using bracken fern (*Pteridium esculentum* subsp. *arachnoideum*) as a model. To this end, twenty samples were collected from an bracken fern occurrence site within a Cerrado Brazilian Savanna conservation area, with ten samples assigned to each preservation method. Each sample consisted of a single frond from an individual plant. Two fronds were collected from each individual, one for each preservation method, each individual spaced at least 2 meters apart. The first preservation method was field preservation, with the immediate storage of samples in liquid nitrogen followed by storage at -20°C in an uninterrupted cold chain, and finally freeze-drying before grinding for extraction. The second method was herborization, by pressing samples between two sheets of filter paper using a botanical press for one month prior to grinding for extraction. The samples were extracted with methanol followed by a liquid-liquid extraction for chlorophyll clean up. The resulting extracts were transferred to vials for HPLC-DAD and UHPLC-MS/MS analysis. The chromatographic pattern of the herborized samples showed that the main phytochemical profile was conserved when compared to the field-preserved samples. While there were changes primarily in the peak intensities of major compounds, no significant new peaks appeared. Thus, the results indicate that herbarium-preserved samples are a promising alternative for plant sample collection in field studies, especially in remote locations.



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Sciforum-207164: Comparative Untargeted LC-MS/MS Metabolic Profiling of Medicinal *Phyllanthus* and *Euphorbia* Species from an Arid Ecosystem

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Arid-zone medicinal plants experience strong environmental constraints, yet their chemical diversity is often described through identified compounds rather than the broader metabolic feature space. We used untargeted LC–MS/MS profiling to compare root, stem, and leaf extracts of four *Phyllanthus* and three *Euphorbia* species collected from western Rajasthan, India. The analysis focused on chemical features shared across species and those associated with individual taxa and tissues. The main *Phyllanthus* dataset contained 39,592 recurrent grouped features, including 7,678 shared across all four species and 11,841 shared among *P. airyshawii, P. amarus, and P. urinaria*. Despite this large common feature pool, 1,034 features showed tissue-associated patterns, indicating differentiation among roots, stems, and leaves. A feature consistent with a hypophyllanthin-like lignan candidate (m/z 453.40607, RT 18.52 min) occurred across all four *Phyllanthus* species and all three tissues, although its identity remains putative. The Euphorbia-containing dataset showed substantial chemical differentiation within the 2–25 min chromatographic region, with 2,756 positive- and 1,806 negative-mode tissue-associated features. Species-associated feature pools were also evident among *E. hirta, E. jodhpurensis*, and *E. thymifolia*. Chemical overlap extended across genera, including 21 features shared between *P. maderaspatensis and E. hirta*. A substantial fraction of recurrent features remained unannotated. Together, these results reveal a combination of shared chemical background, tissue partitioning, and species-associated chemical diversity across arid-zone *Phyllanthus* and *Euphorbia*, providing candidate features for further MS/MS-based structural characterization. Although many LC-MS features remained unannotated, these unresolved signals represent an important part of the plant dark metabolome and may contain ecologically relevant metabolites not yet well represented in public spectral resources. The study highlights the value of LC-MS feature profiling for exploring tissue-level metabolic differentiation in arid-zone medicinal plants and provides candidate feature groups for future targeted LC-MS/MS validation and compound-level identification.



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Session 3. Advanced Data Analysis and Integration in Metabolomics

Sciforum-181079: MassCube: a Python framework for end-to-end metabolomics data processing from raw files to phenotype classifiers

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MS-based nontargeted metabolomics now involves thousands of data files across multiple assays and laboratories. Meanwhile, new mass spectrometers like Orbitrap Astral MS have increased raw data sizes eightfold, demanding more efficient processing. Conventional software, including MS-DIAL, MZmine3, and XCMS, struggles with false-positive peak detection, inefficient in-source fragment handling, and slow computation. MassCube, an open-source Python framework, addresses these challenges with advanced peak detection, adduct/in-source fragment recognition, and high-performance parallel computing. Leveraging array-based programming, MassCube enables scalable, high-throughput analysis for large metabolomics datasets. Systematic benchmarking shows MassCube outperforms leading tools in speed, accuracy, and robustness. MassCube's peak detection was benchmarked against MS-DIAL, MZmine3, and XCMS using both synthetic and experimental LC-MS datasets. In synthetic benchmarking, MassCube achieved 96.5% accuracy, significantly outperforming MS-DIAL (85.4%), MZmine3 (88.4%), and XCMS (87.4%). Experimental benchmarking involved eight LC-MS datasets including human plasma, serum, urine, fecal material, mouse plasma, fruit fly, and plant extracts. A total of 722 manually labeled ion traces were evaluated, with MassCube demonstrating superior accuracy for double-peak (93.5%) and single-peak (97.3%) detection, outperforming MS-DIAL (63.0% and 89.8%), MZmine3 (30.4% and 81.8%), and XCMS (28.3% and 70.3%). Additionally, MassCube exhibited unmatched processing speed and scalability. On a 105 GB Orbitrap Astral dataset, it processed 636 files in 64 minutes on a MacBook M3 Pro (36 GB memory, 12 cores), whereas other software required 8–24 times longer. The framework effectively handled large datasets while maintaining a low memory footprint, enabling high-throughput metabolomics analysis on standard computing hardware. Its modular, object-oriented design also facilitates rapid integration of new algorithms, making it adaptable for evolving metabolomics workflows.



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Sciforum-189085: Leveraging Artificial Intelligence-Driven Metabolomics to Discover Novel Anti-Cancer Therapies

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Recent developments in omics platforms have generated large datasets that offer unprecedented opportunities for data mining and discovery. Among omics, metabolomics yields an immediate, functional readout of tumor biology and cellular state. Despite that, its integration into oncological research continues to fall behind genomics and transcriptomics. This delay is largely driven by a scarcity of extensive patient cohorts, compounded by technical hurdles in measuring diverse metabolites across wide dynamic ranges. For example, distinct metabolites require unique extraction protocols, whereas metabolomics cannot be run on archived tissues, since flash freezing is required, and paraffin-embedding is the most common method of tissue storage. Consequently, expanding access to large metabolomic repositories remains a critical priority for the field.

To bridge this data gap, we established a machine learning framework incorporating statistical models, deep learning architectures, and generative AI. Our strategy relies on two main pillars: (1) synthesizing realistic metabolomic profiles and (2) predicting metabolic abundance directly from transcriptomic signatures. Deploying this pipeline allowed us to identify patterns of tumor metabolic reprogramming associated with patient survival, and pinpoint distinct metabolic vulnerabilities across specific cancer subtypes. Crucially, these computationally prioritized targets were experimentally verified *in vitro* using targeted pharmacological and genetic perturbation assays.

In summary, this work presents a suite of computational tools that resolve longstanding bottlenecks in metabolomics, offering actionable pathways toward target discovery in oncology.



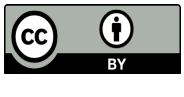
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Sciforum-193026: Network-based integration and interpretation of large-scale public metabolomics datasets using iDMET and iDMET+

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An increasing number of metabolomics datasets have become publicly available in repositories such as MetaboLights and Metabolomics Workbench. Integrating these datasets across studies may provide biological insights that are difficult to obtain from individual studies alone. One major challenge in integrating metabolomics datasets across studies is that peak areas are often not directly comparable between studies. In addition, different analytical platforms frequently target different subsets of metabolites, resulting in limited overlap among detected metabolites. Even if only absolute quantitative measurements are used, only a small number of metabolites are commonly measured across studies. To address these challenges, we developed iDMET, a network-based approach for integrating metabolomics datasets. Each dataset is represented as a differential metabolomic profile consisting of metabolites that are increased or decreased between two groups. Rather than directly comparing peak areas across studies, iDMET identifies similarities between differential metabolomic profiles and constructs an integrated network based on pairwise comparisons of differential metabolomic profiles. We also developed iDMET+, an enrichment analysis framework for the biological interpretation of the resulting network. To evaluate the utility of iDMET, we applied it to 27 publicly available cancer metabolomics datasets. The resulting network revealed known cancer-associated metabolic alterations across multiple studies and identified relationships between datasets that were not apparent from individual studies alone. Furthermore, iDMET+ identified biologically meaningful metabolite sets and generated hypotheses that were not readily obtained using conventional pathway analysis. These results demonstrate that iDMET and iDMET+ provide a practical framework for integrating and interpreting large-scale public metabolomics datasets.



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Sciforum-194535: From 600 to 100 MHz: Developing Reliable Benchtop NMR Protocols for Urine Metabolomics

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Metabolomics enables comprehensive analysis of low-molecular-weight metabolites, reflecting the interaction between genetic and environmental factors. Nuclear Magnetic Resonance (NMR) spectroscopy is valued for robustness, reproducibility and minimal sample preparation. However, high-field instruments (600 MHz) are costly and infrastructurally demanding. Low-field benchtop NMR instruments (100 MHz) represent a cost-effective alternative for point-of-care applications. This study describes the development and validation of optimized urine metabolomics protocols for benchtop NMR.

Urine samples collected from healthy volunteer were processed using lyophilization (1.2 mL aliquots, 18 h), followed by reconstitution in D_2O with phosphate buffer. WET solvent suppression was applied for ^1H NMR acquisition at 100 MHz; parallel spectra at 600 MHz served as reference. Lyophilization duration (6, 18, 24 h), buffer concentration (1.5-4.5 M), and three preparation procedure were evaluated. Metabolite kinetic stability was monitored over 2.5 days, and storage conditions (25°C, 4°C, -80°C, and -80°C after reconstitution in D_2O) were assessed at 24 h, 48 h, 1 week, and 1 month. Data were analyzed by Principal Component Analysis following spectral binning and normalization.

Eighteen hours of lyophilization achieved optimal water removal. WET suppression improved metabolite detectability at 100 MHz. Reconstitution in D_2O caused isotopic exchange of labile protons and minor chemical-shift variations; H_2O reconstitution yielded spectra closely matching non-lyophilized samples. The 3 M phosphate buffer provided the best buffering capacity. Kinetic analysis identified time-dependent spectral changes in creatinine and citrate, which were excluded from further analyses. Orbital shaking (5 min) followed by centrifugation (5 min, 4°C) showed the highest reproducibility. Results at 100 MHz and 600 MHz were substantially comparable.

This work establishes a reproducible analytical pipeline for urine metabolomics at 100 MHz. The optimized protocol ensures spectral quality, analytical reproducibility, and sample stability, supporting the translational potential of benchtop NMR for point-of-care metabolomics.



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Sciforum-195248: TG-ME-Met: An Integrative Transformer-Graph Variational Autoencoder Framework for Multi-Modal Characterization of Tumor Microenvironments through Spatial Transcriptomics and Metabolomics

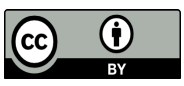
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The tumor microenvironment (TME) is a complex ecosystem of malignant, stromal, and immune cells whose spatial organization influences tumor progression, therapeutic response, and clinical outcomes. Although spatial transcriptomics has enabled detailed characterization of cellular heterogeneity, integrating additional molecular layers is essential for a more comprehensive understanding of tumor biology. Here, we present **TG-ME-Met**, an extension of the Transformer-Graph Microenvironment Explorer (TG-ME), a multi-modal computational framework that combines transformer architectures, Graph Variational Autoencoders (GraphVAE), and metabolomics integration to characterize tumor niches. TG-ME-Met integrates spatial transcriptomics, morphological imaging, metabolomics, multi-omics datasets, molecular interaction networks, and other biological data sources.

The framework employs a multi-stage pipeline including data normalization, spatial integration, morphological feature extraction, gene expression quantification, metabolite profiling, single-cell characterization, and tumor niche identification. The transformer module captures complex molecular interactions, while the GraphVAE incorporates spatial neighborhood information to identify biologically meaningful microenvironmental structures. Application of TG-ME to high-resolution non-small cell lung cancer (NSCLC) datasets revealed distinct microenvironments associated with disease severity and progression. The framework identified multiple biologically relevant niches, including hypoxia-, epithelial-mesenchymal transition (EMT)-, apoptosis-, interferon alpha-, interferon gamma-, TNF-alpha-, and E2F-associated tumor regions. These niches exhibited molecular signatures linked to tumor aggressiveness, immune regulation, metastasis, and therapeutic resistance. In addition, tumor-stroma interfaces showed enrichment of inflammatory, immune, coagulation, and MAPK-related pathways.

By integrating metabolomics with spatially resolved transcriptomic and imaging data, TG-ME-Met provides a systems-level understanding of tumor ecosystem organization and function. This approach enables the identification of molecular and metabolic programs associated with specific tumor niches and disease progression. Future applications will focus on uncovering metabolomics-driven microenvironments and biomarkers associated with prognosis and treatment response, advancing precision oncology through comprehensive multi-modal characterization of the TME.



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Sciforum-195688: Penalised Mixed Effects Modelling of Longitudinal Metabolomics Data

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Introduction: The Earlybird study is a cohort study of children which investigated the development and determinants of insulin resistance in childhood (1). Data were collected at 12 annual visits and longitudinal serum NMR-spectroscopy metabolomics data were available for 130 participants. Analysis of metabolomics data is complicated by the large number of variables, causing overfitting and instability in standard mixed effects regression. One-at-a-time approaches to modelling metabolite variables fail to account for between-metabolite relationships (2). Missing data is a common issue in longitudinal studies.

Methods: A multilevel least absolute shrinkage and selection operator (LASSO) model was used to perform variable selection (3). Penalisation allows the simultaneous analysis of a large number of predictors that would not be feasible with standard regression. This method has rarely been applied to longitudinal metabolomics data. Random forest multiple imputation was used to estimate missing values. Models included adjustments for age, sex and BMI SD score.

Results: Multilevel LASSO regression was applied across 20 multiply imputed datasets, with insulin resistance as the outcome. Sixteen of the metabolite variables were selected in ≥75% of the multilevel LASSO regression models across the imputed datasets and retained for further analysis. Six of the selected metabolomics features showed statistically significant negative pooled associations with insulin resistance.

Conclusions: A multilevel LASSO modelling approach is applicable to longitudinal metabolomics data, and a reproducible analysis workflow has been established. The approach handles high-dimensional sets of predictors where standard regression is not feasible, manages missing data via multiple imputation, and models individual trajectories over time via random effects. Next, performance of the modelling procedure will be formally evaluated in a simulation study. Preliminary results from the simulation study will also be presented if available.

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Sciforum-195755: Toward Interpretable Multi-Omics Biomarker Discovery in Breast Cancer: A Meta-Analytic Framework Integrating Attention-Based Deep Learning, Deep Transfer Learning, and Contrastive Learning

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Introduction: Identifying clinically meaningful biomarker signatures from complex, multiplatform metabolomics data remains a major challenge in precision oncology. Although individual platforms provide complementary insights into breast cancer biology, an integrated framework for subtype-specific feature extraction and biologically interpretable biomarker discovery remains limited. Building on previous work in lipidomic reprogramming, pan-subtype metabolic fingerprinting, and HER2-focused multimodal integration, this study presents a computational framework for breast cancer biomarker discovery.

Methods: Breast cancer tissue metabolomics data from the METAcancer cohort were harmonized across LC–MS, GC–MS, and NMR platforms. After matching samples across all three platforms, the dataset comprised **253 tissue samples** with **183 LC–MS, 161 GC–MS, and 180 NMR metabolite features**. Training data were subsequently oversampled to address class imbalance. A feed-forward artificial neural network with feature-level attention was used to prioritize subtype-discriminative metabolites. Selected features were analyzed using an ANN-based transfer-learning architecture with platform-specific autoencoders to derive compact cross-platform latent representations. Encoder-derived contributions were mapped to individual metabolites, and SHapley Additive exPlanations (SHAP) provided class-specific, directionally resolved interpretation. Contrastive representation learning was incorporated to refine subtype-aware latent representations.

Results: The framework integrates complementary metabolic signals across platforms while retaining metabolite-level interpretability. The HER2-rich profile is characterized by elevated phosphatidylcholine species PC 30:1, PC 32:1, and PC 32:2, and phosphatidylethanolamine PE 32:1, together with higher contributions from N-acetyl-D-mannosamine, glutamine, taurine, and aspartic acid. Selected triacylglycerol (TAG) species show reduced contributions. SHAP-based attribution provides subtype-resolved interpretation of these HER2-associated metabolic signatures.

Conclusions: This framework integrates attention-based feature prioritization, ANN transfer learning, contrastive representation learning, oversampling, and SHAP interpretation to translate heterogeneous multiplatform metabolomics into biologically interpretable HER2-associated candidate biomarkers and testable hypotheses for precision oncology.



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Sciforum-195807: A structure-aware platform for comprehensive lipidomics annotation and quantification

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Current lipidomics pipelines struggle with extensive lipid structural diversity and limited coverage. We present an end-to-end intelligent analysis platform that integrates annotation and rapid quantitative analysis in a platform-independent software solution. It incorporates a mixture-of-experts (MoE) model that jointly learns mass spectral information and lipid structural features to enable structure-aware spectral interpretation, Crucially, it uniquely achieves seamless compatibility with both electron-activated dissociation (EAD) and Paternò–Büchi (PB) derivatization spectra—a capability not offered by any existing platform—alongside conventional MS/MS. It also features a manually curated 972.1-million-entry dynamic lipid fragmentation library, designed to maximize structural coverage across conventional and emerging lipid space by incorporating diverse fatty-acyl chain acylation patterns, sulfated and amino-acid-conjugated bile acids, lipid A species, glycolipids, and emerging lipid classes. The platform delivers ultra-fast spectral searching and high annotation accuracy (MedRE $<$0.3%, FDR 5.7%). The platform also features a rapid, accurate, and reproducible quantification module, enabling streamlined lipid quantitation across diverse acquisition modes and experimental designs. Leveraging its unique PB compatibility, we identified lipid isomer markers that robustly distinguish breast cancer, benign breast nodules, breast cancer lung metastasis, and primary lung cancer—discrimination unattainable by other methods due to their inability to jointly process PB and EAD spectra. This platform significantly advances comprehensive lipidomics analysis.



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Sciforum-196090: Mapping phytochemicals and neuroprotective mechanisms in five medicinal plants: a knowledgebase-driven approach

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Neurophytochemistry is a growing research area that studies bioactive metabolites and signaling mediators in plants for potential neurotherapeutic applications. Phytochemicals can modulate the CNS homeostasis by modulating the activity of neurotransmitter receptors systems, such as γ-aminobutyric acid (GABA), serotonin, and dopamine. They can also promote neuronal survival by enhancing brain-derived neurotrophic factor (BDNF) expression, inhibiting nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)-mediated neuroinflammation, and activating the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway to enhance cellular antioxidant defenses, thereby attenuating oxidative damage, mitochondrial impairment, deficits in neurotrophic signaling, apoptotic pathways, and protein misfolding and aggregation. Advancing phytomedicine applications hinges on a deep understanding of these hallmark pathological processes.

An integrated database of phytochemicals constituents was developed for the following five medicinal plants with reported neuroprotective and cognitive potential (*Melissa officinalis, Salvia officinalis, Rubus ulmifolius, Hypericum perforatum,* and *Papaver rhoeas*). Data on phytochemical occurrence, chemotaxonomy, molecular descriptors, mechanistic evidence, blood-brain barrier (BBB) permeability, gastrointestinal stability, bioaccessibility, microbial biotransformation, and level of experimental evidence were obtained through systematic literature mining and manual expert curation.

The database currently includes 46 species-specific metabolites from the selected taxa. The metabolites are primarily flavonoids, phenolic acids, terpenoids, prenylated phloroglucinols, naphthodianthrones, and alkaloids. The majority are associated with antioxidant activity, while some are associated with anti-inflammatory molecular mechanisms. Evidence of BBB permeability, however, is limited and data on microbial biotransformation requires further refinement. This database links phytochemical occurrence with molecular descriptors, providing a framework that will support candidate prioritization as it grows. Overall, the database will aid in feature annotation metabolite prioritization detected by untargeted LC-QTOF-MS/MS, enhancing the interpretability of future metabolomics studies.



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Sciforum-196091: Enabling subcellular DESI-MSI for broad adoption: Acquisition through to analysis

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Advances in the acquisition and analysis of spatial proteomics and spatial transcriptomics data have been transformative, leading to their wide adoption by researchers. Due to this popularity, standardized sample preparation, data acquisition, and analysis pipelines are becoming more common and accessible for these techniques. However, spatial metabolomics workflows tend to be more specialized across laboratories, and thus less accessible to the broader research community. The bespoke nature of spatial metabolomics is particularly evident in ultra-high spatial resolution mass spectrometry imaging (MSI), where analysis at the cellular and subcellular level is difficult to interpret, computationally intensive, and often requires specific, expensive hardware additions for acquisition.

Here, we will present the development of hardware and software solutions to democratize the acquisition and analysis of cellular and sub-cellular MSI. Our approach involves 1) acquisition of cellular and sub-cellular MSI data at 1 x 1 and 2 x 2 µm using a minimally adapted desorption electrospray ionization (DESI)-XS source, and 2) end-to-end analysis with our novel, open-source software package, MSI.EAGLE. Starting with an unprocessed mass spectrometry image (MALDI or DESI) in open .imzML format, an H&E stain of the same tissue, and consumer-grade compute, we demonstrate the ability to link cellular and sub-cellular metabolic information to cell provenance with our workflow. The entire analysis can be completed without difficult or expensive hardware modifications, without writing a single line of code, and using only open-source software. By lowering the barrier to entry in this manner, we hope to bring the state of high-resolution spatial metabolomics closer to other spatial omics techniques in its accessibility to researchers.



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Sciforum-197188: Integrated HPLC–MS and NMR Data Fusion Improves Diagnostic Precision in Pediatric Chronic Kidney Disease

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Introduction: The diagnostic strategies needed for chronic kidney disease and congenital uropathies in children should be minimally invasive, clinically feasible and detect early metabolic changes. This pilot study evaluated whether integration of targeted HILIC–MS/MS and ^{1}H NMR urine profiling improves the discrimination of children with renal impairment associated with congenital uropathies from controls.

Methods: A single-point prospective diagnostic pilot study included 47 pediatric urine samples collected at initial diagnosis: 22 children with vesicoureteral reflux grades II–V and 25 controls with no urinary tract disease. The mean age of the cohort was 2.5 ± 2.2 years. For HILIC–MS/MS analysis, urine samples were analysed using a Shimadzu LC-20AD system coupled to a Sciex 4500 QTRAP mass spectrometer in positive electrospray Scheduled MRM mode. For ^{1}H NMR analysis, urine samples were acquired on a 500 MHz Bruker AV III spectrometer using a 1D NOESY sequence. Metabolite concentrations were normalized to creatinine. Missing values did not exceed 5% and were imputed using Bayesian PCA. PCA, discriminant analysis, PLS-DA, leave-one-out cross-validation, and high-level data fusion were applied.

Results: Low sensitivity and high specificity for group separation obtained from the HILIC–MS/MS model, 57% and 91%, respectively. The greatest contribution was from the following variables: tryptophan, phenylalanine, and trimethylamine N-oxide. The ^{1}H NMR data additionally showed partial separation of the groups; the metabolites most responsible for this separation included anserine and homovanillate. Data fusion of HILIC–MS/MS and ^{1}H NMR outputs resulted in enhancement of the classification balance for 80% sensitivity and 92% specificity.

Conclusions: In this pediatric pilot cohort, urine metabolomics using combined HILIC–MS/MS and ^{1}H NMR was more informative for the diagnostic classification than single-platform analysis. The novelty of the work is the use of multimodal, creatinine-normalized urine metabolite profiling and data fusion in congenital-uropathy-associated renal impairment in children, resulting in an enhancement of sensitivity without loss of the high specificity.



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Sciforum-204038: Metabolomic Profiling of Botanical Ingredients by ^{1}H NMR for Quality Evaluation ofNatural Health Products

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The chemical composition of botanical natural health products can vary considerably due todifferences in plant species, geographic origin, cultivation and processing conditions, and storagepractices. Such variability can affect product quality, consistency, and authenticity, highlightingthe need for comprehensive and reliable analytical strategies for the characterisation of botanicalingredients. Metabolomics based on proton nuclear magnetic resonance (^{1}H NMR) spectroscopyprovides a non-destructive, reproducible, and efficient approach for the simultaneous detectionand characterization of multiple metabolites in complex plant matrices.

Non-targeted Nuclear Magnetic Resonance (NMR) spectroscopy provides a comprehensivespectral fingerprint representing numerous metabolites within a botanical sample. Such metabolicfingerprints can be used to assess species identity and evaluate metabolite consistency amongbotanical ingredients. However, there remains a gap in published research regarding the structuralelucidation and identification of bioactive molecules represented within NMR spectral fingerprintsof many botanical species.

The objective of this research is to develop NMR-based metabolite fingerprint profiles combinedwith structural elucidation of bioactive molecules from selected botanical species used asingredients in natural health products. This approach is intended to establish a comprehensivequality assurance workflow in which a single NMR analysis can provide three complementarylevels of information: (i) verification of botanical species identity, (ii) assessment of productconsistency through metabolite fingerprinting, and (iii) verification and structuralcharacterization of bioactive molecules of interest. The proposed NMR-based approach haspotential to support improved authentication, quality evaluation, and standardization of botanicalingredients used in natural health products



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Sciforum-204192: Integrated Metabolomics and Genome-Scale Metabolic Modeling Reveal Metabolic Rewiring in Inflammatory Bowel Disease

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Inflammatory bowel disease (IBD) is characterized by chronic intestinal inflammation resulting from complex interactions among host genetics, immune dysregulation, environmental factors, and the gut microbiota. Although microbial dysbiosis has been consistently associated with IBD, the metabolic mechanisms linking microbial activity to host immune responses remain poorly understood. This study presents an integrative systems biology framework combining multiomics data and genome scale metabolic modeling (GEM) to investigate host-microbiome metabolic interactions underlying IBD pathogenesis.

Fecal and peripheral blood samples will be collected from patients with IBD, healthy controls, and dextran sulfate sodium (DSS) induced murine colitis models. Community level GEMs of the gut microbiota will be constructed. Plasma metabolomic profiling will quantify short chain fatty acids, bile acids, amino acid derivatives, and other microbiota derived metabolites. Peripheral blood mononuclear cell transcriptomes will be analyzed and in parallel, publicly available colonic epithelial and fibroblast transcriptomic datasets (GSE277964) will be integrated to generate cell type specific GEMs representing Crohn's disease, ulcerative colitis, and healthy tissues. Predicted microbial metabolite fluxes will subsequently be incorporated into host metabolic models to simulate metabolic cross talk between the gut microbiota and host cells.

This study establishes a comprehensive computational framework for integrating metagenomics, metabolomics, transcriptomics, and GEMs to investigate host-microbiome interactions in IBD. Beyond characterizing disease associated metabolic alterations, this approach provides a platform for mechanistic hypothesis generation and precision nutrition or microbiome-targeted therapeutic strategies. The resulting systems level models will offer a valuable resource for future translational studies and personalized metabolic interventions in inflammatory bowel disease.



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Sciforum-205852: Alterations in Plasma Lipidomics Signatures During Progression of Metabolic Dysfunction-associated Steatotic Liver Disease Towards Hepatocellular Carcinoma

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Metabolically Dysfunctional-associated Steatotic Liver Disease (MASLD) is a spectrum of diseases that starts with the accumulation of excessive fat within the hepatocytes of healthy individuals, leading to liver inflammation and can progress to advanced scarring (cirrhosis), Hepatocellular Carcinoma (HCC), and liver failure. Common radiologic tests and serum-based surrogate markers are used; however, operator dependence, radiological exposure, and affordability are major limitations. Furthermore, while liver biopsy is the gold standard for MASLD staging, it is significantly limited by its invasiveness, sampling variability, and potential interobserver variability. Thus, finding novel non-invasive markers for diagnosis and prognosis is necessary.

Lipids and metabolites play a significant role in the remodelling of MASL to its more severe forms. In this study, we performed comprehensive global plasma lipidomics profiling of non-MASLD healthy individuals, MASLD, and HCC patients. Plasma samples were subjected to liquid-liquid extraction using a cold methanol and dichloromethane (MeOH/DCM) protocol developed in laboratory with previous modifications. Profiling was performed utilising a Vanquish UHPLC system coupled to an Orbitrap mass spectrometer with an HSST3 column. The platform operated in positive and negative polarity with an Orbitrap resolution of 120,000 and a scan range of 70–1500. Analytical stability was monitored by injecting a quality control (QC) sample at the beginning of the batch and after every 10 experimental samples. Data processing and lipid identification were conducted using Compound Discoverer by employing strict screening criteria, including QC, high mass accuracy and MS2 scores.

We performed systematic comparisons of MASLD, Cirrhosis and HCC patients from healthy individuals to observe substantial alterations in lipid classes, such as Sphingolipids, glycerolipids and phospholipids, which were strongly associated with MASLD stage and disease severity to hold significant promise for development as non-invasive diagnostic and prognostic markers for predicting disease severity and establishing clinico-pathological correlations.



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Session 4. Clinical Metabolomics and Drug Metabolism

Sciforum-206562: NMR-Based Metabolomics Reveals Diabetes-Associated Metabolic Dysregulation in Early-Stage Chronic Kidney Disease

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Impact:

This study identifies important metabolic pathways and potential biomarkers for early diagnosis and disease monitoring by revealing diabetes-associated metabolic dysregulation in early-stage chronic kidney disease (CKD). In order to delay the progression of chronic kidney disease (CKD) and lessen complications related to diabetes, these findings promote precision medicine approaches, tailored treatment interventions, and better risk assessment.

Motivation:

Type 2 diabetes mellitus (T2DM) is a primary cause of chronic kidney disease (CKD), accelerating disease development via oxidative stress and complex metabolic disruptions. However, the metabolic mechanism underlying diabetes-associated renal damage in the early stages of CKD are poorly understood.

Aim:

This study used serum ^{1}H NMR-based metabolomics to assess metabolic changes in early-stage CKD patients with and without type 2 diabetes. It also sought to discover possible biomarkers and disrupted metabolic pathways linked to diabetic CKD.

Method:

^{1}H NMR spectroscopy was used to assess serum samples from 100 people with early-stage CKD, including patients with and without T2DM. Metabolic pathway analysis was used to discover impacted biochemical pathways after multivariate and univariate statistical approaches were used to find significantly changed metabolites.

Results:

Patients with diabetic and non-diabetic chronic kidney disease (CKD) showed different metabolic profiles; lower levels of citrate, serine, and methionine suggested problems with energy metabolism and one-carbon metabolism; pathway analysis showed notable changes in the tricarboxylic acid (TCA) cycle and amino acid metabolism, indicating the metabolic impact of diabetes in early CKD.

Conclusion:

The three metabolites that were identified—methionine, citrate, and serine—may be useful biomarkers for the early identification and description of diabetic chronic kidney disease (CKD), assisting with better risk assessment and individualized treatment plans.



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Sciforum-207307: Quality-Control and Quality-Assessment of Metabolomics Workbench

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Introduction: While depositing omics data into public repositories is frequently required by grant funders and journals, the quality of deposited data is not uniform, limiting its reuse in large meta-analyses. Here we present a comprehensive evaluation of data quality across all publicly available datasets in Metabolomics Workbench.

Methods: We downloaded 7240 datasets from Metabolomics Workbench in July 2026. Needed harmonizations and repairs were made to downloaded analysis files.

For each dataset, we attempted to:- convert to a summarized experiment R object containing metabolite metadata, abundances, and sample metadata;- detect any quality-control samples;- determine if the data were log-transformed;- evaluate the number of metabolite features and usable samples in each group of subject-sample-factors (SSF);- calculate sample-sample information-content-informed Kendall- (ICI-Kt) correlations;- calculate the relative standard deviations (RSD) within each SSF group;- perform principal component analysis (PCA) and calculate an analysis of variance (ANOVA) for sample PC scores based on SSF groups.

For each successful step, we assigned a color-based data quality grade: **red**, think twice before using; **yellow**, probably OK; and **green**, looks good for that step. In addition, we generated an HTML QC/QA report for each of the datasets.

Results: Of the 7240 datasets that could be parsed, 167 (2.3%) could not be coerced into a summarized experiment object for various reasons; 622 (8.6%) had $<$3 samples, and therefore could not undergo PCA and RSD calculations; another 5 (0.069%) started correlation but could not complete all steps, and 6446 (89%) were able to go through all steps to PCA. For successful PCA, 333 had either a single SSF, or every sample was its own SSF, making them inappropriate for differential analyses. Among the 6113 remaining, 2053 (34%) had all **green** statuses; 2077 (34%) had one or more **yellow** statuses; and 1983 (32%) had one or more **red** statuses across the QC/QA evaluations.



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Sciforum-162943: From Plasma Metabolites to Therapeutic Targets: Translational Prioritization of Metabolic Pathways in Intervertebral Disc Degeneration

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Background: Intervertebral disc degeneration (IVDD) is increasingly recognized as a metabolic disease involving profound alterations in cellular metabolism, yet translating metabolomic discoveries into clinically actionable targets remains a major challenge. We sought to identify circulating metabolic pathways associated with IVDD and establish a translational framework linking plasma metabolites to candidate therapeutic targets.

Methods: Eighty genetically predicted plasma metabolites and metabolite ratios were systematically evaluated for associations with cervical IVDD, thoracic/thoracolumbar/lumbosacral IVDD (TTL_IVDD), and low back pain using a two-sample Mendelian randomization approach. Prioritized metabolic signals were subsequently integrated with effector-gene annotation and DrugBank to construct metabolite–gene–drug relationships with potential clinical relevance.

Results: Two plasma metabolites remained significant after multiple-testing correction, both for TTL_IVDD. Higher genetically predicted dimethylarginine (SDMA + ADMA), linked to DDAH1, was associated with reduced disease risk, whereas higher alpha-hydroxyisovalerate, linked to LDHA, was associated with increased risk. Additional suggestive associations implicated glycolysis, mitochondrial metabolism, one-carbon metabolism, and amino acid metabolism in IVDD pathogenesis. Importantly, integrating effector-gene annotation with DrugBank connected these metabolite-associated pathways to pharmacologically tractable targets, identifying multiple annotated compounds interacting with DDAH1 and LDHA. This integrative strategy extended metabolite discovery beyond association analysis by providing biologically interpretable and therapeutically relevant molecular targets.

Conclusions: Our study identifies phenotype-specific metabolic pathways underlying IVDD and establishes a translational metabolomics workflow that connects circulating metabolites to effector genes and pharmacologically tractable targets. This metabolite–gene–drug framework facilitates biological interpretation of metabolomic findings, prioritizes candidate therapeutic targets, and provides a scalable strategy for translating metabolomics into precision medicine.



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Sciforum-167705: Identification of Metabolic Marker Profile and Study on Metabolic Pathway Regulation in the Progression of Non-Alcoholic Steatohepatitis to Hepatocellular Carcinoma

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Objective: Non-alcoholic steatohepatitis (NASH) is a major risk factor for hepatocellular carcinoma (HCC), whereas the metabolic reprogramming features and regulatory mechanisms underlying disease progression remain unclear. This study combined human clinical specimens and staged SD rat NASH-HCC animal models to screen stage-specific metabolic markers separately from two cohorts and uncover core metabolic regulatory pathways, so as to supply metabolomic evidence for early diagnosis and targeted therapy of NASH-associated HCC.

Materials and Methods: Human samples including 32 simple steatosis, 45 fibrotic NASH, 28 early carcinogenesis and 50 HCC cases, alongside staged SD rat specimens (n=15 per subgroup) were enrolled. UPLC-MS/MS-based untargeted and targeted metabolomics was performed on human and rodent samples respectively. Differential metabolites were independently screened in human and animal cohorts via OPLS-DA and fold change analysis, and cross-species consistently altered metabolites were summarized. Pathway enrichment and PPI analysis were conducted separately for two datasets using MetaboAnalyst and STRING. An 8-biomarker diagnostic panel was built based on human metabolomic data and assessed with internal cross-validation. LO2 and HepG2 cell lines were used for functional verification of pivotal metabolites.

Results: A total of 127 differential metabolites were identified from combined human and rat data, among which 36 displayed consistent dynamic variation across full NASH-HCC progression in both cohorts, including sphingosine-1-phosphate, taurocholic acid and L-arginine. The diagnostic model based on eight human-derived metabolites yielded an AUC of 0.923 (95%CI: 0.876-0.961) after cross-validation to distinguish early carcinogenesis from fibrotic NASH. Parallel pathway analysis in two cohorts validated that disrupted lipid metabolism, abnormal amino acid metabolism and reprogrammed energy metabolism dominated disease progression. Cellular assays validated that sphingosine-1-phosphate facilitates hepatocyte proliferation and invasion via PI3K/Akt activation.

Conclusion: Using paired human and animal specimens, this study defines metabolic disturbance patterns during NASH-to-HCC transition and establishes a high-performance metabolic signature for staged diagnosis. The synergistic carcinogenic regulation of lipid-amino acid-energy metabolic network is clarified, providing novel metabolomic targets for risk stratification, early screening and precision intervention of NASH-related HCC.



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Sciforum-177933: Metabolomic Signatures of Polyphenol Intervention in Non-Alcoholic Fatty Liver Disease: Pathway-Level Insights into Lipid and Energy Metabolism

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Introduction:

Non-alcoholic fatty liver disease (NAFLD) is characterized by profound disturbances in lipid and energy metabolism. While polyphenols have demonstrated therapeutic potential in improving clinical markers of NAFLD, their metabolomic impact remains incompletely characterized. This study aimed to systematically evaluate metabolomic alterations associated with polyphenol interventions in NAFLD and identify key metabolic pathways underlying therapeutic responses.

Methods:

A PRISMA 2020-compliant systematic review was conducted using PubMed, Scopus, and Web of Science databases (2015–2025). Randomized controlled trials and metabolomics-based clinical studies investigating polyphenol supplementation in adult NAFLD patients were included. Studies employing mass spectrometry or NMR-based metabolomic profiling were analyzed. Identified metabolites were categorized into lipidomics, amino acid metabolism, bile acid metabolism, and energy-related pathways. Pathway enrichment analysis was performed using reported metabolite alterations.

Results:

Seventeen studies met inclusion criteria, including nine clinical trials with metabolomic endpoints. Polyphenol supplementation was consistently associated with modulation of acylcarnitines, decreased saturated free fatty acids, and normalization of phosphatidylcholine/phosphatidylethanolamine ratios. Significant reductions in circulating ceramides and diacylglycerols were reported, indicating improved lipid homeostasis. Alterations in branched-chain amino acids and tricarboxylic acid cycle intermediates suggested enhanced mitochondrial function. Several studies demonstrated shifts in bile acid composition and increased short-chain fatty acid production, reflecting gut–liver axis modulation. Pathway analysis identified significant regulation of AMPK-mediated energy sensing, β-oxidation pathways, and inflammatory lipid mediator synthesis.

Conclusions:

Polyphenol interventions induce measurable metabolomic remodeling in NAFLD, particularly within lipid and energy metabolism pathways. The consistent modulation of ceramides, acylcarnitines, and bile acids suggests potential metabolomic biomarkers of therapeutic response. These findings support the integration of metabolomics into nutritional intervention trials to enable precision-based strategies for metabolic disease management.



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Sciforum-189887: The effect of antibiotics on the metabolism of nosocomial MDR strains of *Klebsiella pneumoniae*: exemplified by phenyllactic acid. *In vitro* experiment.

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Introduction

High levels of phenyllactic acid, a bacterial metabolite, in the blood are a poor prognostic factor, indicating the progression of multiple organ dysfunction and an increased risk of mortality in patients with sepsis and septic shock. *Klebsiella pneumonia (K. pneumoniae)* is a key pathogen in hospital-acquired infections that lead to multiple organ failure and are characterized by a high incidence of antibiotic resistance. Therefore, there is growing interest in the metabolic adaptations of bacteria in response to antimicrobial agents.

Methods

To isolate the MDR strain of *K. pneumoniae*, a primary culture of clinical material was performed. Eppendorf tubes were placed with 1 ml of thioglycollate medium, 50 µl of a 24-hour *K. pneumoniae* culture suspension, a disk soaked in antibiotic solution, and incubated at 37°C for 24 hours. The phenyllactic acid concentration in the resulting suspension was then determined by gas chromatography-mass spectrometry.

Results

The experiment examined the effects of 14 broad-spectrum antibiotics on the metabolic activity of nosocomial MDR *K. pneumoniae* strains. Our results demonstrate the heterogeneous response of *K. pneumoniae* to antimicrobials, highlighting that antibiotic exposure does not always suppress bacterial metabolism. Three clear patterns were identified: strong metabolic suppression, metabolic stimulation (a significant increase in metabolism with certain antibiotics), and intermediate effects (when metabolism is not altered by antibiotics). The obtained results are in good agreement with the classical method of assessing the sensitivity of *K. pneumoniae* strains to antibiotics.

Conclusions

Thus, changes in phenyllactic acid production may reflect reorganization of metabolic pathways associated with resistance mechanisms. The results of quantitative assessment of *K. pneumoniae* metabolic activity demonstrate the potential for personalized antimicrobial therapy. Continued research in this area will open opportunities for optimizing clinical selection of antimicrobial agents based on the metabolic characteristics of bacterial strains.



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Sciforum-190685: Decoding NAFLD Through Microbiome-Associated Metabolomics and Metabolic Phenotypic Expression

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Background: Non-alcoholic fatty liver disease (NAFLD) is a progressive metabolic liver disorder strongly associated with gut microbiome-associated metabolic dysfunction. This study aimed to identify serum metabolomic signatures associated with NAFLD severity using untargeted metabolomics.

Methods: Serum samples were collected from healthy controls (HC, n = 19), non-alcoholic fatty liver (NAFL, n = 16), non-alcoholic steatohepatitis (NASH, n = 10), and cirrhosis patients (CH, n = 6). Untargeted metabolomic profiling was performed using gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-time-of-flight mass spectrometry (LC-TOF-MS). Multivariate chemometric and pathway enrichment analyses were conducted to identify disease-associated metabolic alterations.

Results: A total of 105 metabolites were identified across all study groups. Distinct metabolic profiles were observed among HC, NAFL, NASH, and CH cohorts. Short-chain fatty acids (SCFAs), including acetate, butyrate, and propionate, were significantly reduced in NAFLD patients, whereas cholic acid, palmitoylcarnitine, and L-carnitine levels were elevated in advanced disease stages. Pathway analysis revealed perturbations in butanoate metabolism, primary bile acid biosynthesis, fatty acid degradation, and energy metabolism pathways. Multivariate analyses demonstrated clear metabolic segregation among disease groups.

Conclusions: NAFLD progression is associated with profound serum metabolomic alterations involving reduced microbiome-associated SCFAs, dysregulated bile acid metabolism, and impaired mitochondrial β-oxidation. These findings provide insight into gut-liver metabolic interactions underlying NAFLD progression and identify potential circulating metabolic biomarkers associated with disease severity.

Significance: Distinct serum metabolomic signatures were identified across NAFL, NASH, and CH. Altered SCFA, bile acid, and acylcarnitine metabolism highlighted dysregulated gut-liver metabolic pathways associated with NAFLD severity.



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Sciforum-191425: Metabolomic Signatures of Parental Obesity in Childhood Obesity

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Childhood obesity has a multifactorial etiology, involving a complex interplay between endocrine, nutritional, environmental, perinatal, socioeconomic, and psychological determinants. Of these, the family history of obesity stands out as one of the most significant risk factors for the development of obesity in offspring. In this regard, both maternal and paternal obesity have been documented as factors that may trigger programming mechanisms that may result in elevated metabolic risk throughout the lifespan. Furthermore, the intergenerational transmission of parental obesity may occur through lifestyle, as children from families with obesity frequently exhibit a tendency towards unhealthy dietary habits and sedentarism. However, the molecular mechanisms underlying this predisposition remain to be elucidated. In this study, we investigated whether a correlation exists between parental obesity and the presence of persistent metabolic alterations in children with obesity. To this end, a cohort of obese children has been recruited, comprising those with and without parental obesity, in addition to healthy control children. Blood samples were collected for biochemical and inflammatory analysis, while the characterisation of the circulating metabolites was assessed through untargeted metabolomics using a high-throughput LC-MS method. The results indicated that parental obesity was associated with unhealthier metabolic outcomes in children, as evidenced by elevated fasting insulin levels and impaired insulin sensitivity. This was accompanied by alterations in multiple obesity-related metabolic pathways, such as energy homeostasis, amino acid metabolism, oxidative stress, synthesis of steroid hormones and bile acids, membrane lipid composition, and exposome-related metabolites. Notably, some differential metabolites exhibited more pronounced changes in children with parental obesity, especially at the erythroid level, when compared to counterparts without parental obesity. Therefore, we hypothesise that family history of obesity could be an important factor in modulating and exacerbating the characteristic metabolic impairments that typically underly childhood obesity.



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Sciforum-193373: Cord Blood Metabolomic Profiling Reveals Fetal Reprogramming in Intrauterine Growth Restriction

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Introduction: Intrauterine growth restriction (IUGR) alters fetal metabolic programming, increasing the risk for immediate neonatal complications and long-term health complications. The exact biochemical shifts underlying this are not fully understood. Umbilical cord blood reflects the fetal metabolic environment at birth. To compare IUGR and appropriate-for-gestational-age (AGA)/healthy pregnancies, we employed untargeted metabolomics on umbilical cord blood for identifying metabolic signatures and disrupted metabolic pathways to better understand fetal growth restriction and guide future postnatal interventions.

Methods: Following informed maternal consent, a matched case-control study was conducted comprising 30 IUGR and 30 AGA pregnancies. Fresh umbilical cord blood samples were obtained at delivery, and whole blood samples were analyzed for untargeted metabolomics using gas chromatography-mass spectrometry. The area-under-the-curve values for metabolites obtained after noise reduction and elimination of reaction intermediates were processed in MetaboAnalyst 6.0. Univariate and multivariate analyses, as well as pathway enrichment analysis, were used to identify potential biomarkers and disrupted metabolic pathways.

Results: Univariate and multivariate models revealed a significant metabolic shift, with significant elevations of cholesterol, 2-ketoglutaric acid, L-5-oxoproline, and pyruvic acid and downregulation of 1-monopalmitin in the cases. Receiver Operating Characteristic Curve evaluations established a 5-biomarker panel with a diagnostic area under the curve of 0.946. Enrichment analysis revealed severe disruption of lipid homeostasis, with steroid and cholesterol biosynthesis showing statistical enrichment. Pathway analysis showed that hypercholesterolemia is associated with mitochondrial energy metabolism, severely impairing the TCA cycle and glyoxylate metabolism.

Conclusions: Cord blood metabolomics effectively differentiates IUGR from AGA pregnancies, uncovering significant fetal metabolic reprogramming characterized by dysregulated lipid homeostasis and redirected steroidogenesis, coupled with mitochondrial metabolic impairment. The identified 5-metabolite panel demonstrates exceptional discriminatory power, offering a highly promising, clinically translatable biochemical foundation to complement standard diagnostic tools for identifying pathologically growth-restricted fetuses and for identifying early therapeutic targets to mitigate the long-term metabolic consequences of IUGR.



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Sciforum-193378: Characterization of Intra- and Extracellular Metabolic Profiles by ^{1}H NMR in Aβ1-42-Treated Human Astrocytes from Healthy and Alzheimer's Disease Subjects

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Alzheimer's disease (AD) is the leading cause of dementia and is characterized by progressive neurodegeneration, synaptic dysfunction, and metabolic impairment. Astrocytes play a critical role in maintaining brain homeostasis and are increasingly recognized as active contributors to AD pathophysiology, yet the metabolic changes underlying their dysfunction remain incompletely understood. In this study, we established an optimized Nuclear Magnetic Resonance (NMR)-based metabolomics workflow to profile both intracellular (endo-) and extracellular (exo-) metabolomes of primary human astrocytes derived from healthy subjects (HS) and AD patients. Cells were exposed to oligomeric $A\beta_{1-42}$ to model amyloid-induced stress. Using ^1H NMR spectroscopy at 600 MHz, we quantified 40 intracellular and 33 extracellular metabolites, enabling a comprehensive assessment of astrocyte metabolic responses. $A\beta_{1-42}$ treatment induced metabolic alterations in both HS and AD astrocytes, particularly affecting energy metabolism and amino acid pathways. Notably, intracellular phosphocreatine levels decreased consistently, suggesting impaired energy-buffering capacity under stress. AD-derived astrocytes also showed reduced β-alanine levels, potentially reflecting altered antioxidant defense mechanisms. Analysis of conditioned media revealed distinct extracellular responses, with AD astrocytes exhibiting increased levels of metabolites linked to tricarboxylic acid cycle activity and amino acid metabolism, whereas HS astrocytes displayed changes consistent with altered substrate utilization.Although none of these differences remained statistically significant after correction for multiple testing, likely due to the limited sample size, the observed trends are biologically plausible and provide preliminary insights into astrocyte metabolic adaptations to amyloid stress.Overall, this work establishes a robust and reproducible NMR-based workflow for integrated endo- and exo-metabolomic analysis of human astrocytes. The findings highlight the potential of metabolomics to uncover subtle metabolic alterations relevant to AD and provide a foundation for future studies in larger, well-characterized cohorts.



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Sciforum-195501: PRESERVATION FLUID FTIR FINGERPRINTING AS A PRE-IMPLANT READOUT OF EARLY KIDNEY GRAFT FUNCTION

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Introduction: Delayed graft function remains a clinically relevant early complication after kidney transplantation and reflects, at least in part, the cumulative biological stress experienced by the graft before implantation. Current risk assessment relies mainly on donor, recipient and perioperative variables, but these parameters may not fully capture the biochemical status of the organ at the end of static cold storage.

Objectives: To investigate whether Fourier-transform infrared spectroscopy (FTIR) of kidney preservation fluid can provide a rapid pre-implant biochemical fingerprint associated with delayed graft function.

Methods: In this retrospective proof-of-concept study, preservation fluid samples from 56 kidney transplants were analyzed using a dried-film FTIR workflow. Spectral modelling focused on the 900–1800 cm^{-1} fingerprint region, including phosphate- and carbohydrate-associated signals within approximately 900–1200 cm^{-1} and the amide II and amide I domains at approximately 1500–1600 cm^{-1} and 1600–1700 cm^{-1}, respectively. Spectral variables were selected independently within each donor-blinded training fold rather than from a fixed preselected band panel. Three predictive strategies were compared: a clinical model based on conventional variables, an FTIR-only model, and a combined clinical-plus-FTIR model.

Results: Delayed graft function occurred in 14 of 56 transplants. The FTIR-only model achieved the highest discrimination, with an area under the receiver operating characteristic curve of 0.814. The clinical model reached an AUC of 0.775, while the combined model reached an AUC of 0.796. These findings suggest that preservation fluid contains measurable biochemical information related to early graft function, not fully captured by standard clinical variables alone.

Conclusions: FTIR fingerprinting of kidney preservation fluid may offer a fast, low-volume and scalable approach for pre-implant graft assessment. Although exploratory, these results support further multicenter validation and recalibration before clinical implementation.



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Sciforum-195564: Untargeted Metabolomics Reveals Bile Acid and Tryptophan Metabolic Signatures Associated with Lenvatinib Resistance in Hepatocellular Carcinoma Patients

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Background: Lenvatinib is a first-line targeted therapy for advanced hepatocellular carcinoma (HCC), but acquired resistance frequently develops, limiting long-term efficacy. The underlying metabolic reprogramming remains poorly understood. This study aimed to identify plasma metabolic signatures associated with lenvatinib resistance using untargeted metabolomics. Methods: A total of 46 advanced HCC patients treated with lenvatinib monotherapy were enrolled. After 3 months of treatment, patients were classified according to mRECIST criteria as responders (complete or partial response, n=22) or non-responders (stable or progressive disease, n=24). Pre-treatment plasma samples were collected and analyzed by ultra-high-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). Multivariate statistical analyses including principal component analysis (PCA) and orthogonal partial least squares discriminant analysis (OPLS-DA) were performed to identify differential metabolites. Pathway enrichment analysis was conducted using MetaboAnalyst. Results: A total of 127 differential metabolites were identified (VIP$>$1.5, p$<$0.05, fold change $>$1.5 or $<$0.67). Bile acid and tryptophan metabolism were the most significantly enriched pathways. Compared with responders, non-responders showed significantly elevated levels of primary and secondary bile acids including glycocholic acid (GCA), taurochenodeoxycholic acid (TCDCA), and deoxycholic acid (DCA) (all p$<$0.01). Additionally, tryptophan-derived metabolites such as kynurenine and kynurenic acid were markedly increased, while serotonin was decreased in the resistant group (all p$<$0.05). A combined panel of three metabolites (GCA, kynurenine, and DCA) predicted lenvatinib resistance with an area under the curve (AUC) of 0.89 (95% CI: 0.79–0.96). Conclusions: Dysregulated bile acid and tryptophan metabolism are closely associated with lenvatinib resistance in HCC patients. These identified metabolic signatures may serve as predictive biomarkers and offer potential targets for overcoming resistance.



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Sciforum-195608: Dynamic Metabolomic Profiling Reveals Bile Acid and Lipid Metabolic Remodeling Associated with Pathological Response to Neoadjuvant Chemotherapy in Pancreatic Ductal Adenocarcinoma

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Background: Neoadjuvant chemotherapy (NAC) is increasingly used in borderline resectable and locally advanced pancreatic ductal adenocarcinoma (PDAC), yet metabolic remodeling underlying pathological response remains poorly characterized. This study aimed to identify dynamic plasma metabolic signatures associated with response to NAC using untargeted metabolomics. Methods: A total of 44 PDAC patients receiving NAC (FOLFIRINOX or gemcitabine-based regimens) were enrolled and classified as responders (major or complete pathological response, n=20) and non-responders (minimal or no response, n=24) according to the CAP tumor regression grading system. Paired plasma samples were collected before NAC initiation and after NAC completion (pre-surgery). UHPLC-MS/MS-based untargeted metabolomics was performed. Differential metabolites and pathway enrichment were analyzed using multivariate statistics and MetaboAnalyst. Results: A total of 152 differential metabolites were identified (VIP$>$1.5, p$<$0.05). Bile acid and glycerophospholipid metabolism were the most significantly enriched pathways. Responders exhibited a marked decrease in primary and secondary bile acids including cholic acid (CA), chenodeoxycholic acid (CDCA), and deoxycholic acid (DCA) after NAC (all p$<$0.01), while non-responders showed minimal changes. Additionally, responders demonstrated significant remodeling of lipid metabolites, with decreased phosphatidylcholines (PCs) and increased sphingomyelins (SMs) following NAC (all p$<$0.05). A panel combining baseline and post-NAC changes of CA and PC(34:1) predicted pathological response with an area under the curve (AUC) of 0.91 (95% CI: 0.82–0.97). Conclusions: Dynamic metabolomic profiling reveals that bile acid and lipid metabolic remodeling is closely associated with pathological response to NAC in PDAC. These findings may facilitate early identification of responders and guide treatment optimization.



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Sciforum-195612: Untargeted Metabolomics Reveals Bile Acid and Lipid Metabolic Signatures Associated with Gemcitabine Resistance in Cholangiocarcinoma Patients

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Background: Gemcitabine-based chemotherapy is the standard first-line treatment for advanced cholangiocarcinoma (CCA). However, drug resistance frequently develops, leading to poor prognosis. The metabolic alterations underlying gemcitabine resistance in CCA remain poorly understood. This study aimed to identify plasma metabolic signatures associated with gemcitabine resistance using untargeted metabolomics. Methods: A total of 52 advanced CCA patients treated with gemcitabine plus cisplatin were enrolled. After 3 months of treatment, patients were classified according to RECIST criteria as responders (partial response or stable disease, n=26) and non-responders (progressive disease, n=26). Pre-treatment plasma samples were collected and analyzed by UHPLC-MS/MS-based untargeted metabolomics. Multivariate statistical analysis (OPLS-DA) and pathway enrichment were performed. Results: A total of 143 differential metabolites were identified (VIP$>$1.5, $p<0.05$). Bile acid metabolism, glycerophospholipid metabolism, and tryptophan metabolism were the most significantly enriched pathways. Compared with responders, non-responders showed significantly elevated levels of conjugated bile acids including taurocholic acid (TCA) and glycodeoxycholic acid (GDCA) (both $p<0.01$), as well as increased lysophosphatidylcholines (LPCs) ($p<0.05$). Additionally, the kynurenine/tryptophan ratio was markedly higher in resistant patients ($p<0.01$), suggesting enhanced IDO activity. A combined panel of three metabolites (TCA, LPC 18:2, and kynurenine) predicted gemcitabine resistance with an area under the curve (AUC) of 0.91 (95% CI: 0.83–0.97). Conclusions: Dysregulated bile acid, lipid, and tryptophan metabolism are closely associated with gemcitabine resistance in cholangiocarcinoma. These metabolic signatures may serve as predictive biomarkers for chemotherapy response and offer potential therapeutic targets to overcome resistance.



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Sciforum-195867: Urinary Untargeted Metabolomics Identifies Tryptophan-Nicotinamide Pathway Disturbance as an Early Biomarker of Vancomycin-Induced Acute Kidney Injury

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Background: Vancomycin is widely used for treating Gram-positive infections but frequently causes acute kidney injury (AKI), especially in critically ill and postoperative patients. Early detection of vancomycin-induced AKI (VI-AKI) remains challenging due to the low sensitivity of traditional markers. This study aimed to identify urinary metabolic signatures associated with early VI-AKI using untargeted metabolomics. Methods: A total of 60 patients receiving intravenous vancomycin therapy were prospectively enrolled. According to KDIGO criteria, 30 patients developed AKI within 7 days (VI-AKI group) and 30 remained without AKI (control group). Urine samples were collected at baseline (before vancomycin) and at 24 hours after treatment initiation. Samples were analyzed by UHPLC-MS/MS-based untargeted metabolomics. Multivariate analysis (OPLS-DA) and pathway enrichment were performed. Results: A total of 108 differential urinary metabolites were identified (VIP$>$1.5, p$<$0.05). The tryptophan-nicotinamide pathway was the most significantly perturbed. Compared with controls, VI-AKI patients showed significantly decreased urinary levels of tryptophan and serotonin, accompanied by elevated levels of kynurenine, quinolinic acid, and nicotinamide (all p$<$0.01). Notably, changes in the kynurenine/tryptophan ratio and nicotinamide/tryptophan ratio were detectable as early as 24 hours, prior to the rise of serum creatinine. A combined panel of three metabolites (kynurenine, quinolinic acid, and nicotinamide) predicted VI-AKI with an area under the curve (AUC) of 0.93 (95% CI: 0.87–0.98). Conclusions: Urinary untargeted metabolomics reveals that disturbance of the tryptophan-nicotinamide pathway is an early metabolic signature of vancomycin-induced AKI. This panel may serve as a sensitive, non-invasive early warning biomarker to guide vancomycin dosing and prevent renal injury.



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Sciforum-195875: Pharmacometabolomics of ACE Inhibitors in Chronic Kidney Disease: Serum Bile Acids and Gut-Derived Metabolites Predict Antiproteinuric Response

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Background: Angiotensin-converting enzyme inhibitors (ACEIs) are first-line therapy for reducing proteinuria and slowing chronic kidney disease (CKD) progression. However, substantial interindividual variability in antiproteinuric response exists, and the underlying metabolic mechanisms remain unclear. This study aimed to identify serum metabolic signatures, particularly bile acids and gut-derived metabolites, that predict ACEI antiproteinuric response using pharmacometabolomics. Methods: A total of 55 non-diabetic CKD patients with overt proteinuria were prospectively enrolled and treated with ramipril for 12 weeks. According to the reduction in urinary protein excretion, patients were classified as responders (≥50% reduction from baseline, n=28) and non-responders (＜50% reduction, n=27). Baseline serum samples were analyzed by UHPLC-MS/MS-based untargeted metabolomics. Multivariate analysis (OPLS-DA) and pathway enrichment were performed. Results: A total of 126 differential metabolites were identified (VIP＞1.5, $p<0.05$). Bile acid metabolism and tryptophan-related gut-derived metabolites were the most significantly enriched pathways. Compared with responders, non-responders exhibited significantly elevated serum levels of primary bile acids (cholic acid, chenodeoxycholic acid) and conjugated species (glycocholic acid, taurocholic acid) (all $p<0.01$). Additionally, gut-derived metabolites including indoxyl sulfate and p-cresyl sulfate, as well as kynurenine/tryptophan ratio, were markedly higher in non-responders ($p<0.01$). A combined panel of three metabolites (taurocholic acid, indoxyl sulfate, and kynurenine) predicted poor antiproteinuric response with an area under the curve (AUC) of 0.90 (95% CI: 0.82–0.96). Conclusions: Pharmacometabolomics reveals that elevated serum bile acids and gut-derived uremic toxins are associated with reduced ACEI antiproteinuric efficacy in CKD. These metabolic signatures may serve as predictive biomarkers to guide personalized ACEI therapy and highlight the gut-liver-kidney axis in drug response.



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Sciforum-195894: Metabolomics investigation of the deleterious consequences of prenatal alcohol exposure in subjects with fetal alcohol syndrome.

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Prenatal alcohol exposure is associated with a series of physical (cranial malformations, growth deficits, abnormal brain development) and neurological (cognitive and behavioral disorders) alterations, which altogether constitute the characteristic phenotype of the fetal alcohol syndrome. However, the pathophysiology of this condition is poorly understood, which poses considerable difficulties on its diagnosis because of the lack of sensitive and specific biomarkers. Herein, we propose the application of state-of-the-art metabolomics approaches with the aim of getting deeper insights into the specific molecular mechanisms behind this complex disease. For this purpose, we enrolled a cohort of young individuals (6-18 years), comprising both patients affected by fetal alcohol syndrome and healthy controls matched for age (FAS: N = 15, age = 13.1 ± 3.4; CNT: N = 18, age = 13.5 ± 2.7) and sex (FAS: 66.7% males; CNT: 66.7% males), from whom urine samples were collected for subsequent UHPLC-HRMS untargeted analysis. The teratogenic effects of alcohol were mirrored in profound disruptions in a multitude of central metabolic pathways (e.g., energy homeostasis, lipid metabolism, oxidative stress), which could be responsible for the clinical manifestations of this disorder. These metabolomics alterations suggest the existence of presistent biochemical disturbances that may contribute to the long-term clinical manifestations observed in affected individuals. These findings open the door to define novel diagnostic biomarkers and therapeutic targets for more efficient clinical management of fetal alcohol syndrome and related complications.



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Sciforum-195941: From Metabolites to Therapeutics: A Computational Framework for Therapeutic Discovery from Human Urine Metabolites

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The emergence of metabolomics as an important concept is attributed to the abundance of metabolites in urine, association of metabolites with physiological and pathophysiological processes, and the intrinsic benefits offered by the technique. This study focuses on finding significant human urine metabolites and studying the possible protein targets of the metabolites by using in-silico approaches. In all, 5603 urine metabolites were retrieved from HMDB and filtered through ADMET filtering process based on oral bioavailability, drug-likeness, and cytochrome P450 inhibition properties. Computer-based search of the selected urine metabolites revealed 709 metabolites with desirable pharmacological properties. Protein targets were found using SEA database. The identified target proteins were analyzed for interaction between proteins using STRING and Cytoscape software, which resulted in the identification of the key target genes such as CYP1A1, CYP1A2, CYP2C9, CYP3A4, AKR1C3, and JUN. Pharmcological property based screened metabolites were subjected to reverse molecular docking process. The protein complex containing phenylalanylphenylalanine-1S2C showed maximum binding affinity compared to all the other complexes. The stability of selected complexes was confirmed using molecular dynamics simulation performed using GROMACS software. These results demonstrate that metabolites obtained from human urine have the possibility of being biomarkers or a possible therapeutic agent in future.



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Sciforum-195982: Post-therapy metabolic profiles of tuberculosis patients with treatment-cured and treatment-failed outcomes

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Introduction: Despite effective tuberculosis (TB) treatment, approximately 1.5 million individuals still experience treatment failure annually. The drug-induced metabolic effects of TB treatment, particularly after treatment cessation, remain poorly understood. This pilot study investigated post-therapy alterations in the urinary metabolome of drug-susceptible pulmonary TB patients with either cured or failed treatment outcomes.

Methods: A pretest-posttest study design was used, with urine samples collected at diagnosis (pre-therapy) and after treatment cessation (Week 26, post-therapy) from the same patients. Amino acid analysis (gas chromatography-mass spectrometry) and proton nuclear magnetic resonance were applied to characterise metabolic shifts in treatment-cured (n=14) and treatment-failed (n=10) patient groups. Differential metabolites were identified using the Wilcoxon signed-rank test (FDR-adjusted $p < 0.1$), with visualisation by boxplots and line graphs.

Results: Significant metabolic alterations were observed only in the treatment-cured group, with consistent post-therapy changes in fumaric acid, methylamine, and formic acid. Similar but less consistent trends were seen in the treatment-failed group, where variability and limited sample size may have obscured significance. Although not differential in either outcome group, amino acids or related derivatives generally declined post-therapy in the treatment-cured group, with this trend less pronounced in the treatment-failed group.

Conclusion: The observed shifts reflect not only disease resolution but also persistent treatment-related effects, particularly linked to isoniazid. These findings reveal that isoniazid influences the urinary metabolome beyond treatment cessation, regardless of outcome. Overall, the results underscore the intertwined roles of disease resolution, drug exposure, and microbiome interactions in shaping host metabolism after TB treatment.



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Sciforum-196100: Neurobehavioral Sensitization to Sleep Deprivation is Associated with Re-organization of Circadian Metabolic Rhythm

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Sleep deprivation (SD) produces a wide range of acute and chronic physiological effects. Acute SD impairs multiple neurobehavioral functions, including attention and cognition, which can substantially reduce quality of life and may even become life-threatening in situations requiring sustained vigilance, such as long-distance driving. Notably, the neurobehavioral response to SD varies markedly across individuals: while some remain relatively resistant to sleep loss, others exhibit pronounced vulnerability. The molecular mechanisms underlying this inter-individual variability remain poorly understood.

We hypothesized that differences in the dynamic regulation of metabolic rhythms may contribute to these distinct neurobehavioral phenotypes. To test this, we compared the temporal metabolic profiles of 20 age-, sex-, and BMI-matched individuals classified as either SD-resistant (n=10) or SD-vulnerable (n=10). Plasma samples were collected at 4-hour intervals during a baseline day and during 36 hours of total SD and analyzed using UPLC-MS/MS-based metabolomics. We examined metabolite dynamics associated with both homeostatic sleep pressure and circadian rhythmicity.

Metabolic signatures associated with increasing sleep pressure were largely similar between groups, suggesting that the homeostatic metabolic response to sleep loss is largely phenotype-independent. In contrast, circadian analysis revealed substantial phenotype-specific differences following SD. Vulnerable individuals exhibited pronounced reorganization of circadian metabolic rhythms, characterized by increased cycling within one-carbon metabolism and loss of rhythmicity in amino acid and redox pathways. In contrast, resistant individuals showed loss of rhythmicity primarily in purine metabolism.

Together, these findings suggest that resistance to sleep deprivation may involve greater metabolic re-organization in adapting circadian metabolic programs to prolonged wakefulness, whereas vulnerability may reflect a more rigid metabolic organization. These results highlight circadian metabolic regulation as a potential mechanism underlying individual differences in neurobehavioral responses to sleep loss.



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Sciforum-196431: Ventilator-Associated Pneumonia and Aromatic Microbial Metabolites in Patients After Ischemic and Hemorrhagic Stroke

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Background and Aims

Stroke patients, particularly those requiring mechanical ventilation, are at high risk of developing ventilator-associated pneumonia (VAP), which is strongly linked to increased in-hospital mortality. This study aimed to evaluate whether aromatic microbial metabolites, along with stroke type, sex, and age, are associated with the development of VAP and in-hospital mortality.

Methods

This retrospective observational study included 29 adult patients with acute stroke (9 men, 20 women; median age 77 years, range 31–88). Patients were stratified by stroke type: ischemic (n=23) and hemorrhagic (n=6). Serial serum samples (median sampling interval 4 days, IQR 3–7) were analyzed by gas chromatography-mass spectrometry for phenyllactic acid, p-hydroxyphenyllactic acid, p-hydroxyphenylacetic acid, and their sum (Sum 3). The peak Sum 3 value was used as the exposure variable. VAP was defined according to CDC criteria as a new radiographic infiltrate in patients receiving mechanical ventilation for ≥48 hours. Groups were compared using the Mann–Whitney U test and Fisher's exact test.

Results

VAP was associated with 100% in-hospital mortality (7/7) versus 14% (3/22) in patients without VAP (p=0.0001). Peak Sum 3 levels were significantly higher in patients with VAP (median 8.6 [IQR 4.6–15.0] vs 2.8 [IQR 1.6–5.5] μM; p=0.006) and in non-survivors (median 6.8 [IQR 4.8–11.9] vs 2.5 [IQR 1.6–3.7] μM; p=0.001). However, Sum 3 levels did not differ between ischemic and hemorrhagic stroke subtypes (median 3.9 vs. 3.0 μM; p=0.96). Hemorrhagic stroke showed non-significant trends toward higher rates of mechanical ventilation (67% vs. 39%), VAP (50% vs. 17%), and in-hospital mortality (50% vs. 30%). Sex and age were not significantly associated with VAP or in-hospital mortality.

Conclusions

Aromatic metabolite profiling may serve as a useful complement to clinical criteria for the early identification of stroke patients at highest risk of poor outcome. This hypothesis warrants validation in larger prospective cohorts.



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Sciforum-199166: The Kynurenine/Tryptophan Ratio as a Clinical Metabolomic Biomarker in Adults Living with HIV: A Systematic Review

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Introduction: Persistent immune activation and chronic inflammation remain defining features of HIV infection despite effective antiretroviral therapy (ART). The kynurenine-to-tryptophan (K/T) ratio, a surrogate marker of indoleamine-2,3-dioxygenase-1 (IDO1) activity, has emerged as a promising metabolomic biomarker linking immune dysregulation with clinical outcomes. However, its overall clinical significance across the spectrum of HIV infection has not been comprehensively synthesized. This systematic review evaluated the evidence supporting the K/T ratio as a clinical metabolomic biomarker in adults living with HIV.

Methods: A systematic review was conducted according to PRISMA 2020 guidelines through June 2026. Original studies evaluating plasma or serum kynurenine, tryptophan, or the K/T ratio in adults with HIV were included. Cohort, case-control, cross-sectional, and clinical studies were considered. Methodological quality was assessed using the Newcastle–Ottawa Scale and the Joanna Briggs Institute Critical Appraisal Checklist.

Results: Eighteen studies comprising more than 3,500 participants from 12 countries met the inclusion criteria. Across all studies, the K/T ratio was consistently elevated in people living with HIV compared with seronegative controls. Higher K/T ratios were associated with lower $CD4^+$ T-cell counts, higher plasma viral loads, microbial translocation markers (lipopolysaccharide and soluble CD14), and increased inflammatory cytokines, including IL-6 and TNF-α. Although ART significantly reduced K/T values, complete normalization was uncommon, indicating persistent immunometabolic dysfunction despite viral suppression. Elevated K/T ratios were further associated with delayed immune reconstitution, increased mortality, cardiovascular disease progression, liver fibrosis, HIV-associated neurocognitive disorders, depressive symptoms, and immune reconstitution inflammatory syndrome.

Conclusions: The K/T ratio is a robust clinical metabolomic biomarker that reflects persistent IDO1-mediated immune dysfunction in HIV. Its consistent association with disease progression, chronic inflammation, and multiple HIV-related comorbidities highlights its potential for clinical risk stratification and precision medicine.



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Sciforum-201492: Spatial Metabolomics for Deciphering Immune–Metabolic Niches Driving Fibrosis Progression in Metabolic Dysfunction–Associated Steatotic Liver Disease.

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Background:

Metabolic dysfunction-associated steatotic liver disease (MASLD) affects nearly one-third of adults worldwide and is the leading cause of chronic liver disease. Progression to metabolic dysfunction-associated steatohepatitis (MASH) is characterized by inflammation and fibrosis, with fibrosis stage being the strongest predictor of adverse clinical outcomes. Conventional metabolomics cannot resolve metabolic heterogeneity within liver tissue. Spatial metabolomics, particularly mass spectrometry imaging (MSI), enables *in situ* mapping of metabolites while preserving tissue architecture, providing new insight into localized metabolic remodeling during fibrogenesis.

Methods:

A structured evidence synthesis of studies published between 2022 and 2026 was conducted. Primary studies using imaging MSI, spatial multi-omics and integrated transcriptomics in MASLD were critically reviewed. No original experimental data were generated.

Results:

Recent studies show that fibrosis develops within distinct immune metabolic niches rather than uniformly across the liver. Spatial MSI identified localized accumulation of very long chain phospholipids and oxidative lipid species in fibrotic regions. Spatial lipidomics further demonstrated zonal redistribution of triglycerides, sphingolipids, ceramides, and fatty acids during MASH progression, particularly in periportal fibrotic areas. Integrated spatial analyses revealed close association between activated hepatic stellate cells, endothelial cells, extracellular matrix remodeling, and lipid-associated macrophages. Additional findings include altered bile acid and amino acid metabolism, oxidative stress and ferroptosis-related lipid remodeling. However, most studies remain limited by small cohorts, restricted metabolite coverage and limited clinical validation.

Discussion:

Current evidence supports spatially organized immune metabolic interactions as drivers of fibrosis progression. Integrating spatial metabolomics with single-cell and spatial transcriptomics may improve mechanistic understanding, but standardized analytical workflows and larger longitudinal studies are needed.

Conclusion:

Spatial metabolomics provides a promising framework for investigating fibrosis-associated metabolic remodeling in MASLD. Although disease-specific metabolic niches have emerged as potential biomarker candidates, their translation into precision medicine requires rigorous validation in well-designed clinical studies.



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Sciforum-202117: Metabolic stratification of refractory Lennox Gastaut Syndrome and Controlled focal epilepsy using NMR spectroscopy

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Lennox-Gastaut syndrome (LGS) is characterized by multiple seizure type, often refractory and cognitive impairment. Studies have shown biochemical alterations in epilepsy disorder, however, the metabolic differences between refractory and controlled epilepsy remain unexplored. Our study aims to detect the metabolic disparities across LGS, controlled focal epilepsy (CFE) and healthy controls.

Serum samples were analyzed using ^{1}H nuclear magnetic resonance spectroscopy. Multivariate statistics including PCA (Principal Component Analysis) and PLS-DA (Partial Least Square Discriminant Analysis), followed by variable importance in projection (VIP) scoring and univariate analysis were employed to reveal differentially expressed metabolites. Cohen's d effect size analysis was performed to quantify the magnitude of metabolic differences between groups. Impact of anti-seizure medications (ASMs) class and load on metabolome was investigated in the LGS subgroup.

PCA revealed separate clustering and PLS-DA model showed robust performance in classifying the groups. LGS was characterized by elevated glutamate and acetate along with reduced pyruvate, citrate, creatinine, glutamine, glycine, serine, and acetone. Whereas, CFE demonstrated increased GABA, glycine, and acetone, reduced citrate and glutamine while glutamate, pyruvate and creatinine levels were comparable to healthy controls. No significant differences were observed in LGS patients categorized on the basis of ASM.

Refractory LGS is characterized by pronounced disruption of amino acid and energy metabolism, redox homeostasis, neurotransmitter regulation and ketone metabolism associated pathways, in comparison CFE retains features of metabolic compensation. These deviations may provide insight into mechanisms underlying disease severity and therapy resistance through clinically feasible serum metabolomics.



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Sciforum-204980: Metabolomic and Lipidomic Signatures of Spaceflight and Space-Analog Conditions

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Introduction: Spaceflight and space-analog environments expose biological systems to microgravity, radiation, isolation, confinement, and circadian disruption, leading to systemic physiological adaptations that may be captured by metabolomics and lipidomics. However, available evidence remains fragmented across biological models, matrices, analytical platforms, and mission-related stressors. This systematic review aimed to synthesize metabolomic and lipidomic alterations reported under spaceflight, microgravity, and space-analog conditions.

Methods: A PubMed-based systematic review was conducted following PRISMA 2020 principles. Searches combined terms related to metabolomics, lipidomics, spaceflight, microgravity, simulated microgravity, bed rest, hindlimb unloading, astronauts, and space analogs. Original studies were eligible if they reported metabolomic, lipidomic, sphingolipidomic, or multi-omic data including metabolite-level outcomes in humans, mammalian models, or mammalian cells exposed to space-relevant conditions. Reviews, editorials, plant-only studies, microbial-only studies, and studies without metabolomics/lipidomics were excluded.

Results: Twenty-two original studies were included in the qualitative synthesis. Evidence consistently indicated alterations in mitochondrial and energy metabolism, amino acid turnover, lipid remodeling, sphingolipid metabolism, sulfur metabolism, oxidative stress, gut microbiome–metabolome interactions, musculoskeletal adaptation, renal dysfunction, and immune-cell metabolic reprogramming. Human astronaut studies suggested mission-related and sex-specific metabolic adjustments, while animal, bed-rest, hindlimb unloading, and cellular models provided mechanistic insights into tissue-specific responses to microgravity and associated stressors.

Conclusions: Spaceflight and space-analog conditions are associated with convergent metabolomic and lipidomic signatures reflecting multisystem adaptation. These findings support metabolomics as a promising tool for astronaut health monitoring, biomarker discovery, and development of countermeasures for long-duration space missions.



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Sciforum-206169: Investigation of Metabolic Dysregulation in Advanced-Stage Chronic Kidney Disease Using NMR-Based Urinary Metabolomics.

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Abstract

Clinical assessment of kidney function is an integral part of routine medical care. More than 80% of clinical laboratories report an estimated glomerular filtration rate (eGFR) with endogenous markers such as serum creatinine. However, these markers are influenced by several non-GFR determinants. To address this limitation, we employed a ^{1}H nuclear magnetic resonance (NMR) based urinary metabolomics approach to investigate metabolic dysregulation in advanced-stage CKD (ASCKD). Urine samples from stage 4 CKD (S4, n = 22), stage 5 CKD (S5, n = 36), and healthy controls (HC, n = 22) were analyzed. Sixty-one metabolites were identified and quantified through 1D-^{1}H NMR. Statistical analyses showed clear separation in ASCKD and healthy controls (R^2 = 0.91, Q^2 = 0.79) and identified twenty-five significantly altered metabolites. Univariate receiver operating characteristic (ROC) analysis revealed a panel of fourteen metabolites distinguishing S4 from HC and twelve metabolites for distinguishing S5 from HC. Additionally, phenylalanine and mannitol demonstrated strong discriminatory performance (AUC $>$ 0.80) in differentiating S4 from S5. Pathway enrichment and topology analyses revealed significant perturbations in glycolysis/gluconeogenesis, tricarboxylic acid (TCA) cycle, glyoxylate and dicarboxylate metabolism, pyruvate metabolism, and amino acid metabolism. These findings highlight significant disruption of energy and intermediary metabolism in ASCKD. Integration of urinary metabolomics with clinical markers may improve stratification and enable non-invasive monitoring of CKD severity.



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Sciforum-206635: Integrative Clinical Lipid Metabolomics Analysis of Metabolic Characteristics Underlying Hypertrophic Scar Formation After Plastic Surgery

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Objective Hypertrophic scar (HS) is a common plastic surgery complication marked by fibroblast overactivation and excessive extracellular matrix deposition. Existing studies fail to clarify the regulatory mechanism of lipid metabolic reprogramming in scar fibroblasts. This study aimed to identify differential lipid biomarkers and reveal how lipid disturbance drives scar hyperplasia for novel intervention targets.

Methods A prospective case-control design was adopted. Scar tissues, paired normal skin and serial serum samples were subjected to untargeted lipidomics via UPLC-HRMS. Lipid-transcriptome joint analysis built lipid-gene networks, and in vitro human scar fibroblast models verified the roles of ACC, FASN and CD36.

Results Scar tissues exhibited obvious lipid profile remodeling: saturated fatty acids, phosphatidylcholine and ceramides were elevated, whereas polyunsaturated fatty acids and lysophospholipids declined. Altered lipids concentrated in glycerophospholipid, sphingolipid and fatty acid synthesis pathways, correlating positively with scar severity and angiogenesis. Overexpressed ACC/FASN induced lipotoxicity, activating NF-κB/NLRP3 inflammasome to secrete pro-inflammatory factors and boost collagen synthesis. CD36 exacerbated mitochondrial oxidative stress, forming a lipid accumulation-inflammation-fibrosis vicious cycle.

Conclusion Lipid metabolism disorder serves as a core driver of hypertrophic scar formation. The screened lipid molecules can act as non-invasive diagnostic biomarkers. Targeting lipid metabolic pathways represents a promising therapeutic strategy for HS prevention and treatment.



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Sciforum-206828: Integrated NMR-Based Metabolomics and Clinical Profiling for Differential Diagnosis of Gallbladder Cancer and Gallstone Disease.

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Background:

Differentiating gallbladder cancer (GBC) from gallstone disease (GSD) remains a significant clinical challenge due to overlapping clinical manifestations and the limited diagnostic accuracy of conventional clinical parameters. This study aimed to evaluate the diagnostic utility of serum ^{1}H NMR-based metabolomics integrated with clinical profiling for improved differentiation between GBC and GSD.

Methods:

Serum samples were collected from 50 patients with GBC, 50 patients with GSD, and 20 healthy controls. Metabolic profiling was performed using ^{1}H Nuclear Magnetic Resonance (NMR) spectroscopy. Differential metabolites were identified by comparing GBC and GSD metabolic profiles. Metabolomic and clinical datasets were subsequently integrated using Multi-Omics Factor Analysis (MOFA) to assess their relative contribution to disease classification and diagnostic performance.

Results:

Comparative metabolomic analysis revealed significant downregulation of β-glucose, alanine, and carnitine in GBC compared with GSD. MOFA-based integration demonstrated that the metabolomic dataset contributed more strongly to disease discrimination than clinical parameters alone, indicating superior diagnostic performance of NMR-derived metabolic signatures for differentiating GBC from GSD.

Conclusion:

Integrated analysis of ^{1}H NMR-based metabolomics and clinical profiling highlights the superior diagnostic potential of metabolomic biomarkers over conventional clinical parameters for distinguishing GBC from GSD. These findings support the application of NMR-based metabolomics as a promising complementary tool for the early and accurate differential diagnosis of gallbladder diseases.



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Sciforum-206925: Mitochondrial Dysfunction in Patients with Alcoholic Liver Disease and Nonalcoholic Fatty Liver Disease

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Introduction: Mitochondrial dysfunction is implicated in the pathogenesis of chronic liver diseases and is associated with metabolic disturbances and disease progression. This study aimed to investigate serum metabolite profiles reflective of mitochondrial dysfunction in patients with alcoholic liver disease (ALD) and nonalcoholic fatty liver disease (NAFLD).

Methods: Serum concentrations of carnitine and its 29 acylcarnitine derivatives were measured in patients with NAFLD (n=44) and ALD (n=40) at different disease stages, as well as in 14 healthy volunteers. Additionally, we compared acylcarnitine profiles between cirrhotic (irrespective of etiology) and non-cirrhotic individuals. Targeted metabolomic analysis was performed using high-performance liquid chromatography coupled with tandem mass spectrometry.

Results: Significant differences were found between liver disease groups and controls. The ALD and NAFLD groups differed significantly in C10:2 ($p < 0.001$) and C16:1 ($p < 0.009$). At the cirrhosis stage, compared to non-cirrhotic patients, increases were observed for C2, C5-DC, C14, C14-OH, C16, C16:1, C18:1, and C18:2 ($p < 0.05$ for all), while decreases were noted for C3, C4, C5, and C16-OH ($p < 0.05$ for all). Disease progression was associated with significant differences in Child-Pugh classes for C16 ($p = 0.0014$), C16:1 ($p < 0.0001$), and C18:1 ($p < 0.0001$). Statistically significant differences versus controls were observed from Child-Pugh class B onward ($p < 0.001$), with C16:1 also showing a significant increase in class C.

Conclusion: According to our findings, acylcarnitine metabolism is closely associated with hepatic functional status. Differences between ALD and NAFLD are consistent with distinct pathogenic mechanisms. During cirrhosis progression, decreased C3, C4, and C5 indicate impaired mitochondrial fatty acid oxidation, while increased C2 may reflect restricted acetyl-CoA entry into the Krebs cycle. The rise in long-chain acylcarnitines (C16, C16:1, C18:1) with worsening Child–Pugh class supports accumulation of incomplete oxidation products. Taken together, these findings highlight the potential of serum acylcarnitine profiling as a non-invasive biomarker of mitochondrial dysfunction and disease severity in chronic liver diseases.



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Sciforum-206928: Quality control of the culture media during early stages of NK-cell expansion process

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Introduction: Natural killer (NK) cells have emerged as a promising platform for cancer immunotherapy due to their ability to recognize and eliminate malignant cells without prior sensitization or antigen presentation. Monitoring the composition of culture media throughout the expansion process may provide valuable information for process control within a quality-by-design (QbD) framework.

Objectives: This work applies Fourier-transform infrared (FTIR) spectroscopy combined with machine learning to characterize the global molecular signature of culture media used during NK-cell expansion and to discriminate between different culture media formulations, including compositionally similar media.

Methods: NK cells were isolated from umbilical cord blood samples under legal procedures. Cells were cultured in eight-commercially media: M1-M8. Culture media samples were analysed using a Vertex-70 FTIR-spectrometer with HTS-XT high-throughput accessory. Supervised-classification models were developed based on the best 578-features from normalized first-derivative spectra using the Information Gain algorithm.

Results: A k-nearest neighbours (kNN) model achieved an F1-score of 0.725 for classifying the eight media across days 0-27. To evaluate early process monitoring, models were trained using samples from the first nine culture days only. A Naïve Bayes (NB) classifier reached an F1-score of 0.669, indicating that medium identity can be inferred from FTIR spectra at early culture stages. For the closely related media M1, M2 and M3, NB classifiers achieved F1-scores of 0.728 (days 9-20) and 0.731 (days 0-9).

Conclusions: The results indicate that FTIR-spectroscopy combined with machine learning can successfully discriminate between different culture media used in NK-cell manufacturing, including formulations with similar compositions. Moreover, medium identification is feasible from samples collected during early culture stages, highlighting the potential of this rapid, non-destructive, and cost-effective approach for process monitoring and quality control in NK-cell expansion workflows.



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Sciforum-206953: Early Prediction of Donor-Dependent Expansion Capacity in NK Cells Using FTIR Spectroscopy and Machine Learning

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Introduction: Natural killer(NK) cells are candidates for cancer immunotherapy due to their antitumor-activity and lower risk of graft-versus-host disease than T-cell therapies. However, NK-cell manufacturing is constrained by donor-to-donor variability in expansion capacity, evident after culture days. This limitation reduces opportunities for early-process adjustment, making identification of high-performing donors crucial for improving process efficiency and product consistency.

Objectives: This study combines Fourier-transform infrared(FTIR) spectroscopy and machine-learning to identify molecular signatures in culture media associated with NK-cell expansion potential. The goal is to predict donor-dependent expansion performance at early culture stages, before significant cell-proliferation occurs.

Methods:NK-cells were isolated from umbilical cord blood samples under legal procedures. Culture media samples were analysed using an FTIR-spectrometer across 400–4000cm^{-1}. First-derivative-normalization was applied as a preprocessing method, and supervised classification models were developed using 578 best features from preprocessed spectra, selected using the Information-Gain-algorithm.

Results: Culture samples from ten donors were grouped based on principal component analysis(PCA), generating two donor groups and a third group containing the remaining donors. Using samples collected between days 9 and 20, a k-nearest neighbours model achieved perfect classification (F1-score=1.000). Using early-stage samples (days 0-9), an AdaBoost model achieved an F1-score of 0.896, demonstrating early prediction of donor-related behaviour. Donors were grouped according to a fold-change expansion threshold of 15, generating classes of four and six donors, respectively. For samples collected between days 9 and 20, a Naïve Bayes model achieved an F1-score of 0.958, while an SVM model trained on samples from the first nine culture days achieved an F1-score of 0.867.

Conclusions:FTIR-spectroscopy combined with machine-learning can classify NK-cell donors according to expansion potential, including at early-culture-stages. These findings highlight the potential of this cost-effective approach to support donor selection and process optimization in NK-cell immunotherapy manufacturing.



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Sciforum-207010: Metabolic Signatures of Pancreatic Drain Fluid and Serum in Severe Acute Pancreatitis Revealed by High-Resolution ^{1}H NMR Metabolomics

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Introduction: Acute pancreatitis (AP) is characterized by pancreatic necroinflammation, systemic inflammation, and profound metabolic dysregulation, resulting high mortality and morbidity. The early phase of severe acute pancreatitis (SAP) is accompanied by systemic inflammatory response syndrome (SIRS), multi-organ failure often requiring insensitive support of cardiopulmonary system. Respiratory failure is one of the major complications of AP and most patients with this extremely needed ventilatory support. Although serum metabolomics has been widely explored in SAP, the metabolomic profile of pancreatic drain fluid remains poorly characterized. This study compared the metabolomic signatures of serum and pancreatic drain fluid in SAP using high-resolution ^{1}H NMR spectroscopy.

Methods: Serum samples of SAP patients were collected within 48 hrs of ICU admission, and pancreatic drain fluid samples were obtained within 1-7 days of admission following percutaneous drainage of infected pancreatic collections. A total of 60 samples (30 serum and 30 drain fluid) were analysed using an 800 MHz ^{1}H NMR spectrometer. All the statistical analysis and pathway analysis was carried out using MetaboAnalyst 6.0. Untargeted metabolomic profiling and metabolite identification was done using Chenomx software.

Results: ^{1}H NMR metabolomics identified a different concentration metabolic fingerprint in pancreatic drain fluid compared with serum. Elevated arginine, tyrosine, phenylalanine, histidine, and formate, together with reduced glucose, delineated a compartment-specific metabolic phenotype, underscoring localized metabolic dysregulation associated with severe acute pancreatitis.

Conclusion: Pancreatic drain fluid metabolomics identifies localized metabolic perturbations with the potential to advance biomarker discovery and support precision medicine through improved clinical decision-making in severe acute pancreatitis.



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Sciforum-207362: Development and Validation of a Comprehensive LC-MS/MS Targeted Assay for Uremic Solute Profiling in Chronic Kidney Disease

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Uremic solutes are toxic metabolites derived from endogenous and gut microbial metabolism normally excreted by the kidneys. Their diverse chemical properties present challenges for analytical analysis. A comprehensive uremic solute assay was developed to optimize a workflow to increase coverage of clinically relevant uremic solutes in pediatric Chronic Kidney Disease (CKD). From an initial database of 130 candidates, 25 uremic solutes were selected based on high fold-change significance, etiology, clinical reporting in uremia, and cost. A targeted metabolomics assay was developed using Multiple Reaction Monitoring (MRM) on a Waters TQ-S Micro triple quadrupole mass spectrometer, utilizing both ionization modes. ¬-Chromatographic separation was achieved via a Waters ACQUITY UPLC with a BEH C18 column. Absolute quantification was processed through TargetLynx software using a 15-point calibration curve. Validation was performed in charcoal-stripped human plasma and normalized against internal isotopic standards. Finally, the assay was applied to 22 pediatric CKD samples (healthy to kidney failure). A rapid LC-MS/MS assay using a 7- minute MRM method was developed and validated for the quantification of 18 uremic solutes, including creatinine, hippuric acid, and indoxyl sulfate. This assay validated LOQ utilizing internal standards and charcoal-stripped plasma calibration. Most targeted solute levels of uremic solutes strongly correlate with CKD progression with hypoxanthine as an exception. In conclusion, this assay provides a robust tool to monitor pediatric CKD progression at a mechanistic level.



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Session 5. Advances in Metabolomics Technologies

Sciforum-189001: Fluorine-Tagging Strategies for Amino Acid Detection by Low-Field ^{19}F NMR Spectroscopy

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High-field NMR spectroscopy is a cornerstone of metabolomics; however, the high cost and infrastructural requirements of high-field instruments limit its broader applicability. Benchtop LF NMR spectrometers represent an attractive alternative, though sensitivity and resolution remain major challenges. ^{19}F NMR is particularly attractive for LF NMR, as its large gyromagnetic ratio and wide chemical-shift range, together with the absence of naturally occurring fluorine in biological matrices, allow interference-free analysis.[1–3] Chemoselective tagging strategies reduce spectral congestion and enhance target selectivity in NMR, commonly employing isotope-enriched probes. [4,5] Reactive ^{19}F-tags have shown promise for the identification and quantification of amino acids in complex mixtures by ^{19}F NMR. [1,2] Here, we investigate a ^{19}F-tagging approach specifically designed for compatibility with benchtop ^{19}F NMR, targeting a broad panel of proteinogenic amino acids. Amino acid derivatization is performed with selected F-tags, using DMT-MM as coupling agent in liquid media at near-neutral pH. [6,7] Reaction conditions (pH, buffer composition, temperature, and time) are optimized by both high-field and benchtop ^{19}F NMR spectroscopy. Preliminary results show that selected fluorinated tags yield ^{19}F-labelled amino acid products with well-resolved resonances, detectable and quantifiable on the benchtop spectrometer, supporting the feasibility of this approach at LF. Ongoing work focuses on extending the screening to a wider set of amino acids and evaluating tagging selectivity in more complex mixtures. This study aims to establish a proof-of-concept for targeted amino acid profiling using fluorine-assisted tagging combined with LF ^{19}F NMR, bridging established chemoselective derivatization strategies with emerging benchtop NMR technology and laying the groundwork for accessible metabolomics workflows beyond specialized high-field facilities.

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Sciforum-194452: Beyond conventional matrices: optimization and validation of a targeted metabolomics kit for dried blood spots

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Targeted metabolomics kit-based assays are increasingly used for large-scale quantitative profiling in clinical research, yet their validation is largely limited to conventional matrices, like plasma and serum. Extending their applicability to minimally invasive matrices such as dried blood spots (DBS) requires dedicated optimization and validation. This highlights a rarely addressed methodological gap in targeted metabolomics.

This work describes the optimization of the TMIC MTX MEGA assay for DBS and its analytical characterization through a structured workflow including coverage analysis, matrix comparison, and longitudinal performance assessment. The assay combines reverse-phase liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) and direct flow-injection-MS analysis, enabling broad metabolite coverage across multiple classes. Paired DBS and serum samples from 11 participants in a cardiac rehabilitation study, collected at two timepoints, served as the validation set.

A total of 323 analytes were quantified in DBS and 496 in serum. Principal component analysis confirmed clear matrix-driven separation, reflecting well-characterized biological and pre-analytical differences. Coverage gaps in DBS were systematically attributed to either biological matrix effects or panel-specific analytical limitations. Despite differences in absolute concentrations, Pearson correlation and paired *t*-test (p-value <0.05) analyses demonstrated strong preservation of longitudinal trends both across metabolite classes and at the individual level. Class-specific exceptions were observed for triacylglycerols and metabolites with intracellular contributions, consistent with both analytical and biological factors.

This work provides a replicable framework for adapting the TMIC MTX MEGA assay to DBS, preserving the ability to track metabolic changes over time. These preliminary results position DBS as a viable and minimally invasive alternative for longitudinal metabolic monitoring in clinical settings, thus potentially opening the way for large-scale targeted metabolomics studies.



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Sciforum-195546: AI-Assisted Pancreatic Metabolomics Reveals Metabolic Signatures Associated with β-Cell Dysfunction in Experimental Type 2 Diabetes

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Introduction: Type 2 diabetes mellitus (T2DM) is characterized by insulin resistance and progressive β-cell dysfunction. Pancreatic changes remain incompletely characterized. This study investigated pancreatic metabolic signatures in experimental T2DM and evaluated machine-learning approaches for discriminatory features.

Methods: T2DM was induced in male Wistar rats by a high-fat diet followed by low-dose streptozotocin. Animals were divided into healthy controls (n = 10), diabetic rats (n = 10), and metformin-treated diabetic rats (n = 10). Pancreatic tissues underwent untargeted metabolomic profiling using UHPLC-HRMS. PCA, PLS-DA, and FDR-adjusted statistical testing were performed. Random Forest and XGBoost identified discriminatory features. Robustness was assessed using repeated cross-validation and permutation testing, with feature selection within training datasets to minimize information leakage. Pathway enrichment used KEGG and MetaboAnalyst resources.

Results: A total of 1,186 metabolic features were detected, of which 74 showed significant differences after FDR correction (FDR $<$ 0.05). Multivariate analyses indicated differences among groups. Permutation testing assessed whether PLS-DA discrimination exceeded chance. Diabetic tissue showed alterations in glutamate, branched-chain amino acid, sphingolipid, tricarboxylic acid cycle, and oxidative-stress-related pathways. Ceramide and acylcarnitine species and glutamate-related metabolites increased, whereas citrate, succinate, and selected phosphatidylcholine species decreased. Machine-learning analysis identified ceramide C18:0, leucine, glutamate, and succinate as discriminatory features. Cross-validated performance and permutation-based significance supported candidate signatures, requiring validation in larger independent cohorts.

Conclusions: Pancreatic metabolomics with explainable machine learning identified metabolic signatures associated with the diabetic phenotype. Alterations in amino acid, mitochondrial energy, and sphingolipid metabolism may contribute to pancreatic metabolic dysfunction. Identified metabolites are candidate tissue-level signatures and targets, not established clinical biomarkers. Because pancreatic tissue is not routinely accessible for clinical biomarker testing and the study examined a single time point, longitudinal studies and validation in accessible biospecimens and independent cohorts are required to establish temporal relationships, generalizability, and translational utility.



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Sciforum-195860: Valorization of *Rugulopteryx okamurae* through the elaboration of bioactive-rich and functional extracts: Optimization of extraction conditions and comprehensive characterization by complementary spectrophotometric and metabolomics tools

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The proliferation and coastal accumulation of the invasive alga *Rugulopteryx okamurae* has become a significant environmental and socioeconomic challenge. To mitigate such negative effects, great efforts are being made for the valorization of this biomass through the recovery of added-value bioactive compounds. However, for its effective transfer to the productive sector, the development of sustainable extraction methods and further in-depth characterization of the resulting extracts in chemical and functional terms is crucial to foresee feasible applications. Herein, we applied a Box-Behnken experimental design to optimize an ultrasound-assisted approach for the extraction of beach-cast seaweeds. A series of spectrophotometric assays were then employed to determine the contents of major phytochemical classes (polyphenols, flavonoids, phlorotannins, pigments) and *in vitro* biological properties (antioxidant and anti-inflammatory activity), in combination with cutting-edge metabolomics for exhaustive biochemical profiling. Optimal recovery yields were achieved by sonicating for 45 min at 60 °C, using ethanol (55%, v/v) as extractant at a solvent-to-sample ratio of 25 mL/g. Interestingly, the method greenness was found to be superior to that reported in previous studies, as assessed through the AGREEprep metrics (score = 0.75). These extraction conditions enabled us to recover multiple health-promoting compounds, such as polyphenols (majorly phenolic acids, but also flavonoids, phlorotannins, and bromophenols), carotenoids (e.g., fucoxanthin), phytosterols (e.g., fucosterol), vitamins (majorly retinoids, but also B-group and antioxidant vitamins), polyunsaturated fatty acids (good n-6/n-3 balance), and amino acids (including essential species). As a result of this favorable composition, the extracts were proven to exhibit potent antioxidant and anti-inflammatory activity. Altogether, these findings highlight the potential of the environmentally-friendly and cost-effective ultrasound-assisted extraction method developed here to valorize *R. okamurae* through the elaboration of bioactive-rich and functional extracts.



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Sciforum-196071: High-resolution spatiometabolomics in *Drosophila*: Advancing tissue-specific metabolomics via DESI-Mass Spectrometry Imaging

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Understanding the complex metabolic networks governing development, behavior, and disease in the model organism like Drosophila requires high resolution, tissue specific insights. Traditional metabolomics techniques, such as LC-MS and GC-MS, offer robust quantification but necessitate tissue homogenization destroying crucial spatial architecture and limits to resolve metabolic crosstalk between distinct cell types. Here, we present an optimized Desorption Electrospray Ionization Mass Spectrometry Imaging (DESI-MSI) workflow tailored for the ambient mapping of metabolites and pharmaceuticals across diverse Drosophila tissues. Our protocol demonstrates the simultaneous mapping of metabolites including neurotransmitters, lipids, and central energy pathways at near cellular resolution as well as preserves the native biochemical state of fragile insect tissues while operating under ambient conditions. Here, we discuss the utility of DESI-MSI in resolving distinct metabolic microenvironments within intact tissues, mapping metabolic shifts that are otherwise obscured in bulk tissue lysates. Also, successfully delineating distinct metabolic microenvironments between neuronal and glial compartments within the Drosophila brain sections. Furthermore, we tested our method to a translational pharmacology workflow, tracking the blood-brain barrier penetration and spatial distribution of an exogenous drug treatment, while simultaneously monitoring its localized metabolic rescue effects using dfmr1 mutant flies significantly streamlining the tracking of both small molecule drugs and endogenous metabolites. Ultimately, this methodology establishes DESI-MSI as a spatially resolved toolkit for Drosophila research, unlocking new dimensions in functional genomics, toxicology, metabolic disease modeling, cellular metabolism, neurobiology, and preclinical drug discovery.



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Sciforum-204831: Prediction of Kidney Disease Through the Serum Molecular Signature

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Chronic kidney disease (CKD) is a major global health challenge, associated with increased cardiovascular risk, premature mortality, and substantial healthcare burden. As the disease often progresses asymptomatically, many patients are diagnosed only after significant and irreversible loss of kidney function, limiting the effectiveness of early therapeutic interventions.

This study investigated the potential of mid-infrared (MIR) spectroscopy, to acquire the serum molecular fingerprint, combined with machine learning for the rapid and minimally invasive assessment of CKD. A total of 54 bovine serum solutions mimicking the biochemical profiles of the five CKD stages were prepared by simultaneously varying the concentrations of creatinine, urea, and albumin. MIR spectra were acquired using a high-throughput microplate platform requiring only 5 µL of serum, a volume compatible with collection from a simple finger prick, while allowing the simultaneous analysis of up to 96 samples.

The acquired spectra were used to develop Partial Least Squares (PLS) regression models for key biochemical markers of kidney function. Excellent regression performance was obtained for serum creatinine and urea, with correlation coefficients exceeding 0.85. Furthermore, the same spectral data enabled accurate classification of CKD stages. Random Forest, Extreme Gradient Boosting, and Support Vector Machine models achieved areas under the receiver operating characteristic curve (AUC) above 0.98 when using normalized first-derivative spectra.

These results point to the capability of MIR spectroscopy to simultaneously quantify relevant renal biomarkers and accurately discriminate CKD stages from a single measurement. The proposed approach offers a rapid, low-volume, and high-throughput alternative to conventional laboratory methods, highlighting its potential for integration into future point-of-care systems for kidney disease monitoring and management.



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Sciforum-206979: Lyophilization-based protocol for human plasma and serum metabolomics by benchtop NMR spectroscopy: optimization and validation

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NMR spectroscopy is a key technique in metabolomics, enabling the simultaneous identification and quantification of metabolites and lipoproteins in biofluids. Although high-field NMR (600 MHz) remains the gold standard, low-field or “benchtop” NMR instruments are emerging as cost-effective alternatives for translating metabolomics into clinical practice. However, their application to biofluids can be challenged by inadequate suppression of the intense water signal, which compromises spectral quality and metabolite detection. Here, lyophilization followed by reconstitution in deuterated water was investigated as a sample-preparation strategy to improve benchtop NMR analysis of commercially available human plasma and serum. The optimal lyophilization time for 1.2 mL samples was established at 18 h. A standardized reconstitution protocol using 0.7 mL of 90:10 D_2O:phosphate buffer was developed, including controlled shaking and centrifugation. WET and CPMG-WET sequences were optimized for low-field NMR acquisition, and an automated spectral-processing workflow was implemented. The proposed protocol markedly reduced the residual water signal and improved spectral quality, enabling visualization of metabolite signals otherwise poorly detectable or masked in the original samples. CPMG filtering was preferred to chemical deproteination for attenuating protein signals and improving metabolite visualization, without introducing additional sample-preparation steps. Sample integrity was evaluated at 600 MHz by comparing lyophilized/reconstituted samples with the corresponding original samples. The spectra showed substantial overlap, indicating that the overall metabolic profile was largely preserved. However, some volatile metabolites were lost, while deuteration reactions were observed for trace metabolites such as creatinine. Storage stability was evaluated in triplicate under four conditions at both 600 and 100 MHz, followed by Principal Component Analysis. Room-temperature storage showed the lowest stability, whereas -80 °C after reconstitution showed the greatest stability. Overall, this protocol markedly improved benchtop NMR spectral quality while substantially preserving the metabolic profile of plasma and serum, supporting its potential for metabolomics of blood-derived samples.



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Sciforum-207230: Integrating Metabolomics into the Development of Functional Bee-Based Foods for Healthy Ageing

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Bee-derived products such as bee pollen, bee bread, propolis, and royal jelly represent complex natural matrices containing a diverse range of primary and secondary metabolites with potential nutritional and bioactive properties. Their composition is highly influenced by botanical origin, geographical location, environmental conditions, and processing practices, creating challenges for quality assessment, authentication, and the development of standardized functional food ingredients. Comprehensive metabolomic approaches provide an effective strategy for characterizing this chemical complexity and identifying molecular fingerprint associated with functional properties. Within the Horizon Europe BEE-TECH project, an integrated metabolomics approach is applied to investigate bee products originating from Turkey, Romania, and Germany. Methods-based metabolomics are employed to characterize the metabolic profiles of different bee-derived matrices targeted in BEE-TECH project, including bee pollen, bee bread, propolis, and royal jelly. The generated metabolomic datasets are processed using advanced computational workflows, including peak detection, metabolite annotation, spectral database matching, and multivariate statistical analysis, to identify characteristic metabolic patterns and discriminant features among samples from different geographical origins. The metabolomic profiling strategy enables the detection of a broad spectrum of bioactive metabolites, including phenolic compounds, flavonoids, lipids, amino acids, and other specialized metabolites contributing to the nutritional and functional potential of bee products. Chemometric approaches are applied to evaluate sample variability, identify geographical markers, and establish metabolite signatures related to product quality and authenticity. This research demonstrates the application of advanced metabolomics as a powerful analytical platform for the molecular characterization and valorization of bee-derived resources.

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Sciforum-207261: Volumetric Absorptive Microsampling in Biomarker Analysis: Insights from Targeted and Rapid Microbore Metabolic Profiling Approaches

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Introduction: The aim of the study was to assess the feasibility of volumetric absorptive microsampling (VAMS) in biomarker analysis. Amino acids and biogenic amines were quantified in VAMS Mitra devices, liquid venous blood (blood), and plasma using a LC-MS/MS; additionally, profiled using rapid microbore metabolic profiling (RAMMP).

Methods: Paired finger capillary blood on VAMS, blood, and plasma were collected from eight healthy individuals. For LC-MS/MS, samples were prepared using AccTag derivatization [1] and analyzed using RP chromatography (HSS T3 180 µm, 2.1 mm X 150 mm column; 7.5 min) in ESI+ mode. For RAMMP using LC-QTOF-MS, samples were extracted using methanol protein precipitation; RP chromatography (HSS T3 180 µm, 1 mm X 50 mm column; 3.7 min), ESI+, and DDA modes. Data were analyzed using Skyline, MSDIAL, Simca, and MS-excel.

Results: Comparing the targeted metabolites in the three blood matrices 13 metabolites had a strong correlation (Spearman rank (r_s) $>$ 0.6) between the three blood matrices whilst 15 had an accurate concentration comparison ($<$ 15% mean bias). In RAMMP, blood had 3798 features, VAMS 2342, and plasma 1906. PCA captured discrimination of the three blood metabolic profiles while valid OPLS-DA models confirmed their significance ($p < 0.05$). Sixteen had their highest abundance in VAMS, 14 in blood, and 18 in plasma.

Highlights: In the targeted analysis, VAMS provided quantitative information on several amino acids and biogenic amines similar to conventional matrices. Concentrations of certain metabolites greatly differed in VAMS compared to conventional matrices which may necessitate the establishment of their reference ranges in this matrix. RAMMP showed adoption of VAMS in biomarker research may be dictated by the target metabolites of a research study since specific metabolites are captured in the different blood matrices.



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Sciforum-207282: Mapping the Blood Microsample Metabolome: A Multi-Platform Inter-Laboratory Study

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Blood microsampling (BμS) has emerged as a promising approach for analyzing endogenous metabolites. Different BμS devices are currently available, and although they share similar concepts for sample collection, matrix variations may affect analytical outcomes. While some untargeted studies have been published, research comparing these devices to conventional matrices remains predominantly targeted; notably, there is a lack of studies specifically evaluating the qualitative annotations in untargeted workflows. This study aims to provide a comprehensive metabolic and lipidomic map of three BμS devices, namely Dried Blood Spots (Whatman), Volumetric Absorptive Microsampling (Mitra), and Capitainer cards, benchmarked against traditional plasma and whole blood.1

For this purpose, venous blood, plasma, and BμS samples from ten fasting volunteers were analyzed across five laboratories. Using a multi-platform approach (RP-LC-MS/MS, HILIC-LC-MS/MS, GC-MS, and CE-MS), laboratories analyzed the samples using their own in-house workflow and databases. Manually curated level 1 and 2 annotations were harmonized using RefMet and ChEBI identifiers to access the metabolic and pathway coverage of the different matrices.

A total of 350 metabolites were collectively annotated. High comparability between matrices was observed, with 252 metabolites (72%) detected across all five compared sample types. 20 metabolites were unique to BμS and absent in blood and plasma. Lipidomic analysis identified 37 distinct lipid subclasses, with phosphatidylcholines and sphingomyelins being most abundant. While profiles were largely similar across matrices, some compounds were device-specific, such as unique lipid species captured only by the Capitainer device.

Overall, the results demonstrate that BμS devices provide a highly comparable metabolic and lipidomic coverage to traditional blood samples. Furthermore, this study contributes to advancing the field by providing an initial qualitative reference (indicating presence or absence of metabolites/lipids) for the application of BμS in large-scale metabolic studies.



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Sciforum-207348: Microbial metabolic communities in bio-industries

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Background

Metabolomic approaches could be used for the follow up and the optimization of industrial mixed microbial cultures. The diversity of the catalyst was based on non-aseptic approach, and the population was adjusted by controlling the conditions in the bioreactor e.g. on the basis of the gas emissions out of the reactor. Together with measuring the liquid metabolites, they reflect the activities of the mixed flora as a biocatalyst.

In our earlier studies, the mixed strain fermentation production of lactate was boosted by specific industrial strains and enzymes. Then almost 15% yield was attained from cellulosic side streams, and the maximal production of mannitol from mixed raw materials was about 13%.

Methods

At 36°C and pH 6, 100 kg of food molasses were mixed with 700 liters of water and 15 liters of meat bone meal. The reactor was blended by nitrogen flow, which controlled the mixed population. Selected clostridial strains were added. Elevated production of mannitol was studied in a pilot process using mixed rumen microflora with industrial liver specimen as biocatalysts.

The screening of products was carried out as a metabolomics application. The multitude of reactions in the product broth could be defined and measured by the gas flows and the nucleic magnetic resonance (NMR). This principle was used earlier e.g. in the EU Baltic Sea research project “ABOWE” in 2012-15 (for biochemicals).

Results

The principal lab products from molasses in 100 hours were valeric acid (max 7 mg/ml) and butyrate (max 8 mg/ml). Acetate production reached 9 mg/ml in about 60 hours. These chemicals could be further converted into corresponding alcohols, and productivity could be theoretically elevated by e.g. continuous collection of the products. In a pilot trial with $5m^3$ reactor using rumen microbes, production level of 8,5% (w/v) of mannitol from molasses and industrial liver extract was reached in about 48 hours.

In a consequent experiment microbiologically produced lactate from the molasses or from the hygienically safe mixture of abattoir waste and enzymatically hydrolyzed saw dust could be converted into propionate, butyrate and acetate in 20 hours only. The mixed population was boosted with the Propionibacterium *acidipropionici* strain, accepted as production organism by EFSA (European Food Safety Authority).

Conclusion

The joint metabolic capabilities of undefined mixed microbial cultures (UMC) could be upgraded for various industrial side streams. The follow up of the yields and productivities could be achieved by NMR, for instance. The exploitation of raw materials could be simultaneously measured.

The results indicated the potential of mixed strain fermentation in the production of valuable chemicals. The carrier gases increase options for boosting, accelerating or up regulating the processes. The current approach show potential for converting tedious raw materials into valuable chemicals. The residual fractions could be treated for soil amendments according to the results from the EU project “BioResque” (2023-25).



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Session 6. Plant and Animal Metabolism and Metabolic Modeling

Sciforum-191046: Metabolomic characterization of a pomegranate (*Punica granatum* L.) water extract by LC-QTOF-MS

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Introduction

Pomegranate (*Punica granatum* L.) is a fruit widely grown in the Mediterranean region and is widely recognized for its high content of natural antioxidants, including hydrolysable tannins, flavonoids, and phenolic acids. The present study focuses on the detailed metabolomic profiling of a pomegranate water extract using liquid chromatography.

Methods and materials

The metabolomic profile was determined using Ultra-high performance liquid chromatography coupled to a quadrupole time-of-flight mass spectrometer (HPLC-QTOF-MS) in negative mode.

Results and Discussion

LC-MS/MS analysis revealed a complex polyphenolic profile dominated by hydrolysable tannins, mainly ellagitannin- and gallotannin-derived compounds. Low-molecular-weight constituents included gallic acid (*m/z* 169.0149; MS/MS 125.0252), succinic acid (*m/z* 117.0195; MS/MS 73.0294), and glutaric acid (*m/z* 131.0724; MS/MS 85.0664).

The high-mass fraction was characterized by multiple tannins, including digalloylglucose isomers (*m/z* 483.0795), galloyl-HHDP-hexosides (m/z 633.0751/633.0733; MS/MS m/z 301, 463), trigalloylglucose isomers (*m/z* 635.0852; MS/MS 483, 465, 301), punicalagins α/β (*m/z* 541.0288; MS/MS 301, 275, 249), valoneic acid dilactone derivatives (*m/z* 425.0176), granatin A (*m/z* 799.0645), and galloyl-bis-HHDP-glucoside (m/z 935.0802), all showing fragmentation patterns consistent with sequential loss of galloyl and Hexahydroxydiphenoyl (HHDP) groups.

Simple flavonoids were also detected, including epicatechin (m/z 289.0729), catechin (*m/z* 289.0732), quercetin (m/z 301.0373; MS/MS 179, 151), and cyanidin-3-*O*-glucoside (*m/z* 449.1118; MS/MS 287.0586), along with derivatives such as 3,3′-di-O-methyl ellagic acid (*m/z* 329.0322) and methyl-quercetin sulfate (*m/z* 395.0071; MS/MS 301).

Overall, the MS/MS data confirmed that the sample is highly enriched in ellagitannin and gallotannin-type polyphenols, characterized by characteristic fragment ions at *m/z* 301 (ellagic acid) and *m/z* 169/125 (galloyl units), together with flavan-3-ols and flavonols, supporting fingerprint.

Conclusions

LC-MS/MS analysis showed a polyphenol-rich extract dominated by ellagitannins and gallotannins, supported by characteristic MS/MS fragments (*m/z* 301 and 169/125), with minor contributions from flavonoids.



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Sciforum-191975: Untargeted metabolomics reveals phenology and cultivation-dependent signatures of vasodilatory activity in *Heliopsis longipes* leaves

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Plant metabolomes are highly responsive to developmental and environmental cues; however, the extent to which these metabolomic shifts influence biological activity remains poorly understood in medicinal plants. *Heliopsis longipes* (chilcuague) is a Mexican endemic species whose roots contain affinin, a vasodilatory and antihypertensive alkamide. Despite representing the largest proportion of plant biomass, its leaves remain chemically and pharmacologically underexplored. This study integrated metabolomics, chemometrics, and network pharmacology to investigate how phenological stage and cultivation condition shape metabolomic signatures associated with vasodilatory activity in *H. longipes* leaves. Dichloromethane extracts were obtained from wild and greenhouse-grown plants collected at four phenological stages: vegetative, flowering, fruiting, and defoliation. Untargeted metabolomic fingerprinting was performed using GC-MS and FTIR-ATR, while vasodilatory activity was evaluated in isolated rat aorta. ASCA revealed that the interaction between cultivation condition and phenological stage was the dominant source of metabolomic variation, accounting for 38.2% and 41.6% of the variance in GC-MS and FTIR-ATR datasets, respectively. Wild fruiting-stage extracts exhibited the highest vasodilatory efficacy (E_{max} = 100%; EC_{50} = 404.50 ± 61.30 µg/mL) and a distinct metabolomic signature characterized by differential accumulation of eudesmane-type sesquiterpenes, lignans, and phenylpropanoids. PLS regression (R^2Cal = 0.93) demonstrated a strong association between vasodilatory activity and a multicomponent metabolomic signature rather than a single bioactive constituent. Lutein and β-carotene were identified for the first time at the metabolomic level in *H. longipes* leaves. Bioassay-guided fractionation yielded sesamin, which was consistently detected across all experimental conditions and proposed as a chemical marker. Network pharmacology suggested that the identified metabolites may collectively contribute to vasodilation through modulation of PI3K/AKT/eNOS/NO, NF-κB/MAPK, and Ca^{2+}/PDE/cAMP-cGMP signaling pathways. These findings establish wild fruiting as the optimal harvesting stage and position *H. longipes* leaves as a sustainable source of vasodilatory metabolites with phytopharmaceutical potential.



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Sciforum-192874: Metabolomics for Characterizing Trace Metal Toxicity Responses in Marine Bivalves: Insights from Constraint-Based Metabolic Modeling—A Systematic Review

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Marine bivalves are widely recognized as sentinel organisms for coastal biomonitoring because of their sedentary lifestyle and capacity to bioaccumulate trace metals. Exposure to cadmium, lead, and mercury disrupts key metabolic processes, impairing physiological function. Metabolomics has emerged as a valuable approach for identifying biochemical responses to trace metal toxicity, while constraint-based metabolic modeling (CBMM), including Flux Balance Analysis, has been explored in a limited number of studies to provide mechanistic insights. This systematic review synthesizes current evidence on metabolomic alterations in trace metal-exposed marine bivalves and evaluates application of CBMM in toxicity assessment.

Following PRISMA 2020 guidelines, PubMed, Scopus, Web of Science, and Google Scholar were searched for studies published between 2000 and 2025. Eligible studies investigated metabolomic responses to trace metal exposure in marine bivalves. Reviews, non-English publications, and studies lacking metabolomic analyses were excluded. Study was evaluated using predefined methodological criteria assessing study design, analytical methods, and reporting quality. Metabolic disturbances were synthesized according to affected biochemical pathways.

Of 347 records identified, 289 remained after duplicate removal, and 31 studies met the inclusion criteria. Twenty-six studies reported significant alterations in amino acid metabolism, energy metabolism, oxidative stress, and tricarboxylic acid cycle. NMR-based metabolomics was the most frequently applied platform (19 studies), LC-MS (14), and GC-MS (9). Cadmium was the most investigated trace metal (22 studies), and Mytilus spp. were the predominant study organisms (20). Four studies incorporated CBMM, indicating that its application remains limited despite its potential to complement metabolomic analyses.

Current evidence demonstrates that metabolomics is a robust tool for identifying metabolic biomarkers of trace metal toxicity in marine bivalves. Although only few studies integrated CBMM, these highlight its potential to enhance mechanistic interpretation of metabolomic data. Future research should further evaluate genome-scale metabolic reconstructions alongside metabolomics to strengthen environmental toxicity assessment and ecological risk evaluation.



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Sciforum-192906: Metabolomics-Guided Profiling of *Guadua incana* Londoño Reveals Bioactive Phytocompounds Associated with Reduced HCT-116 Cell Viability

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Bamboo species have been widely used in traditional medicine for the treatment of various diseases. *Guadua incana* Londoño is recognized for its richness in phenolic compounds, particularly flavonoids and hydroxycinnamic acid derivatives. However, the chemical diversity and biological relevance of its metabolome remain largely unexplored. This study employed an untargeted metabolomics approach integrated with Global Natural Products Social Molecular Networking (GNPS2) to characterize the chemical space of *G. incana* leaf extracts, guide the targeted isolation of bioactive metabolites, and assess their effects on HCT-116 cell viability using the MTT assay. Leaf extracts were prepared using 96% ethanol and analyzed by ultra-high-performance liquid chromatography coupled with quadrupole time-of-flight tandem mass spectrometry (UHPLC-QTOF-MS/MS). Metabolite annotation and chemical space exploration were performed through molecular networking analysis using GNPS2. Metabolomics-guided fractionation enabled the targeted isolation of major constituents by centrifugal partition chromatography (CPC), followed by purification using Sephadex LH-20. Structural characterization led to the identification of isoschaftoside (**1**) and a flavonoid-rich mixture (**M1**) containing orientin (**2**), flavone base + 3O, 1MeO, C-Hex (**3**), violanthin (**4**), vitexin (**5**), swertisin (**6**), and flavone base + 3O, 1MeO, O-dHex (**7**). Compound **1** reduced HCT-116 cell viability, exhibiting an IC_{50} value of 13.26 µM after 72 h of exposure, while **M1** decreased cell viability by 94.35% at 50 µg/mL. Integrative metabolomic and biological analyses indicated that these flavonoids are associated with the observed reduction in cell viability. This study provides the first metabolomics-guided characterization of flavonoid glycosides from *G. incana* and demonstrates the value of combining untargeted metabolomics, molecular networking, and bioactivity assessment for the discovery of bioactive natural products. These findings highlight this bamboo species as a promising source of phytochemicals with potential pharmacological and biotechnological applications.



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Sciforum-193394: Comparative Secondary Metabolite Profiles and FTIR-Based Chemical Fingerprinting of Three *Vernonia* Species in Nigeria

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Secondary metabolites constitute an important group of plant-derived compounds with diverse biological activities and potential applications in phytomedicine. This study comparatively evaluated the secondary metabolite profiles and Fourier Transform Infrared (FTIR)-based chemical fingerprints of three Vernonia species (Vernonia amygdalina, Vernonia conferta and Vernonia volkamerifolia) occurring in Nigeria. Leaf extracts were fractionated using hexane, ethyl acetate and ethanol solvents. Qualitative phytochemical screening was conducted using standard phytochemical procedures, while quantitative metabolite determination was carried out using established analytical methods. Data were analyzed using one-way ANOVA at $p < 0.05$, and FTIR spectroscopy was used to characterize the chemical fingerprints of the extracts. The results revealed the occurrence of alkaloids, flavonoids, saponins, tannins, anthraquinones, terpenoids, cardiac glycosides, phenols and steroids, although their distribution varied among species and solvent fractions. Quantitative analysis showed significant interspecific variation ($p < 0.05$) in metabolite concentrations, with V. amygdalina exhibiting the highest flavonoid content (5.22 ± 0.172%), while V. conferta recorded higher concentrations of alkaloids (1.90 ± 0.100%) and saponins (1.85 ± 0.150%). Ethyl acetate and ethanol fractions generally yielded greater metabolite recovery than the hexane fraction, highlighting the influence of solvent polarity on extraction efficiency. FTIR analysis of the ethyl acetate fractions revealed characteristic absorption bands corresponding to functional groups such as C–H, C=O, C=C, C–O and N–H, indicating the presence of diverse classes of bioactive metabolites, including phenolics and flavonoids. The observed differences in metabolite composition and FTIR fingerprints among the three species demonstrate interspecific chemical variability within the genus Vernonia and provide baseline information for plant metabolite characterisation, chemotaxonomic studies, and future pharmacological investigations.



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Sciforum-195797: Metabolomic profiling reveals Hydrogen sulfide-induced alterations in the secondary metabolite production of *Trigonella foenum-graecum* (Fenugreek).

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Hydrogen sulfide (H_2S) plays a crucial role in regulating growth, development, and metabolic processes in various plant systems. The current study emphasises on how H_2S signalling affects the physical and physiological parameters, including the secondary metabolome of *Trigonella foenum-graecum* (Fenugreek) through a spectrophotometric method and untargeted liquid chromatography-high-resolution mass spectrometry (LC-HRMS). Under controlled lab conditions, 15-day-old Fenugreek plants were treated with H_2S and repeated at regular intervals of 5 days up to 60 days. On the 60th day, plants were harvested, physiological parameters were measured and leaf samples were frozen in liquid nitrogen and stored at -80° C for further analysis. Targeted metabolite analysis of leaf samples was performed using UV spectrophotometric method. It was observed that 100μM H_2S treatment was optimal for improving plant physical growth parameters, phenolic content, and flavonoid accumulation, whereas 200μM H_2S was more effective in enhancing photosynthetic pigments and alkaloid content. Preliminary analysis by spectrophotometric method revealed notable alterations in secondary metabolites, such as phenolic compounds, flavonoids, and alkaloids. The current findings suggest that H_2S acts as a potent modulator of plant metabolic pathways involved in secondary metabolite biosynthesis. For a better understanding of the shift in secondary metabolite content in control and H_2S-treated leaf samples, untargeted liquid chromatography-high-resolution mass spectrometry (LC-HRMS) will be performed and presented. The findings of this study can offer new insights into how H_2S influences plant metabolism and deepen our understanding of plant-volatile interactions and their role in specialized metabolic pathways.



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Sciforum-195918: A multifunctional ANL superfamily gene *OsACS* couples oxylipin and phenylpropanoid metabolism

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Introduction The ANL (acyl-CoA synthetase/NRPS adenylation domain-luciferase) superfamily catalyzes adenylation and thioesterification. ACS (acyl-CoA synthetase) enzymes activate fatty acids, but their roles in coordinating distinct pathways remain unclear. The jasmonic acid (JA) pathway is part of the oxylipin network, where OPCL (OPC-8:0 CoA ligase) converts OPC (12-oxophytodienoic acid) to OPC-CoA. Meanwhile, 4CL (4-coumarate:CoA ligase) channels hydroxycinnamates into phenylpropanoids (e.g., lignin). Whether JA directly regulates lignin synthesis or a shared enzyme bridges them is unknown. Here, we identified *OsACS*, a rice gene coupling oxylipin with lignin biosynthesis.

Methods We performed mGWAS for 4-coumaric acid (4-CA, a lignin precursor) in indica rice. Multi-omics integration associated *OsACS* alleles with metabolite and expression traits. Recombinant OsACS was assayed in vitro with 4-CA and OPDA. CRISPR/Cas9 knockout and overexpression lines were phenotyped under dehydration stress. Natural variants were characterized via yeast one-hybrid, EMSA (electrophoretic mobility shift assay), and dual-luciferase assays.

Results mGWAS pinpointed *OsACS*, and phylogenetic analysis placed it close to OPCL and 4CL. OsACS localized to peroxisomes, with expression negatively correlated with phenylpropanoids but positively with jasmonates. In vitro, OsACS converted OPC and OPDA to CoA esters (OPCL activity) and accepted multiple hydroxycinnamates (4CL activity). Knockout mutants accumulated less JA land showed enhanced drought tolerance, whereas overexpressors were hypersensitive. Exogenous 4-CA or JA rescued the phenotype. Under osmotic stress, *OsACS* relocalized to the cytosol and nucleus, with ERF transcription factors binding its promoter. A solo-LTR insertion in the MH63 haplotype reduced promoter activity relative to NIP (*Nipponbare*).

Conclusions *OsACS* is a bifunctional enzyme coupling JA and lignin pathways while negatively regulating drought tolerance. Its stress-induced relocalization may enable metabolic reprogramming. The solo-LTR insertion offers a natural allelic variant for breeding.



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Sciforum-196115: LC-MS/MS-Based Metabolomic Profiling and Antioxidant Potential of *Combretum mellifluum* Flower Extracts

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Introduction: Plant metabolomics is a valuable strategy for investigating the chemical diversity of medicinal species and supporting the annotation of specialized metabolites. Species of the genus *Combretum* are recognized for producing phenolic compounds, flavonoids, tannins, and triterpenoids with biological relevance. However, LC-MS/MS-based studies focused on *Combretum mellifluu*m flowers remain scarce. Therefore, this study investigated flower extracts of *C. mellifluum* using HPLC-DAD and LC-MS/MS, combined with antioxidant, total phenolic, and flavonoid content assays.

Methods: Flowers were subjected to ultrasound-assisted extraction using methanol, acetonitrile, acetone, and a ternary mixture of methanol:acetonitrile:acetone. The extracts were analyzed by HPLC-DAD and LC-MS/MS in positive ionization mode. Metabolite annotation was supported by retention time, precursor ions, MS/MS fragmentation patterns, mass accuracy, spectral similarity scores, DAD responses, and literature data. Antioxidant activity was evaluated by DPPH and ABTS assays, while total phenolic and flavonoid contents were determined by Folin-Ciocalteu and aluminum chloride colorimetric methods, respectively.

Results: Three representative metabolites were putatively annotated: betulin, rutin/rutoside, and pedunculagin. Betulin was assigned as a lupane-type pentacyclic triterpenoid based on the dehydrated ion $[M+H-H_2O]^+$ at *m/z* 425.3777 and product ions related to dehydration and skeletal cleavages. Rutin/rutoside showed $[M+H]^+$ at *m/z* 611.1614 and diagnostic fragments at m/z 465, 303, and 153. Pedunculagin was annotated through the ammonium adduct $[M+NH4]^+$ at *m/z* 802.1103 and product ions consistent with ellagitannin fragmentation. The ternary extract showed the strongest antioxidant performance among *C. mellifluum* extracts, with IC50 values of 14.90 µg/mL for DPPH and 57.69 µg/mL for ABTS, as well as the highest flavonoid content, 73.46 mg RE g^{-1}.

Conclusion: These preliminary findings suggest that *C. mellifluum* flowers contain specialized metabolites with antioxidant potential and support further LC-MS/MS-based studies to expand the chemical characterization of this poorly explored plant matrix.



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Sciforum-199488: Metabolic Profiling and Biochemical Diversity of the Cucurbitaceae Family: Implications for Agricultural and Nutritional Optimization

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The Cucurbitaceae family constitutes a phylogenetically diverse botanical group encompassing major agricultural models, specifically evaluating major species under investigation such as *Cucumis sativus*, *Citrullus lanatus*, and *Cucurbita pepo*. Despite their global agrarian prominence, the intricate molecular mechanisms orchestrating their chemodiversity and phenotypic plasticity remain underexplored. This investigation deploys a comprehensive metabolomic framework across 20 representative species spanning 15 distinct tribes to resolve their complex metabolic architectures.

Employing advanced analytical methods based on ultra-high-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS), high-resolution profiling successfully delineated the spatial-temporal distribution of specialized secondary metabolites across diverse plant tissues. Two prominent chemical signatures were explicitly identified: first, the localized hyperaccumulation of oxygenated tetracyclic triterpenoids (*cucurbitacins B and E*), which act as critical phytoanticipins mediating robust biotic stress mitigation; and second, distinct concentration profiles of bioactive *flavonoid glycosides* governing environmental adaptation across various plant developmental phases. Furthermore, the systematic integration of stoichiometric metabolic modeling mapped network flux dynamics, yielding quantitative predictive insights into secondary metabolite biosynthesis under fluctuating environmental perturbations and elicitor treatments.

These empirical findings significantly advance our fundamental understanding of chemosystematic evolution within Cucurbitaceae and furnish a robust baseline for molecular breeding initiatives. By isolating high-resolution metabolic markers associated with superior nutritional density and heightened stress resilience, this study delivers actionable data for crop improvement, successfully bridging classical phytotaxonomy with predictive metabolic engineering.



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Sciforum-206994: Metabolomic correlation analysis of chemical profiles and anti-inflammatory activity of different species of the genus *Guadua*

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Species of bamboo belonging to the genus Guadua represent one of the most important non-timber forest resources in Latin America due to their ecological, economic, and social significance. Beyond their traditional applications in construction and agro-industry, however, their chemical diversity and pharmacological potential remain largely unexplored. Although previous studies have demonstrated that Guadua leaves are rich in polyphenolic compounds exhibiting promising biological activities, the chemical composition associated with their anti-inflammatory activity remain largely unknown. Therefore, this study aimed to identify metabolites and chemical families associated with anti-inflammatory activity by correlating the metabolomic profiles of leaf extracts from different Guadua species using an untargeted metabolomics approach. Twenty-nine leaf extracts were chemically profiled by ultra-high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UHPLC-QTOF-MS). Anti-inflammatory activity was evaluated using two complementary assays: 1) nitric oxide (NO) scavenging capacity determined by the Griess reaction and 2) inhibition of NO production in lipopolysaccharide (LPS)-stimulated RAW 264.7 macrophages. Metabolomic profiles were integrated with biological activity data using multivariate chemometric approaches to identify metabolites and chemical families putatively associated with anti-inflammatory activity. The untargeted metabolomic analysis revealed high chemical diversity among the species evaluated, characterized mainly by flavonoid glycosides, hydroxycinnamic acid derivatives, and other polyphenolic compounds. Biological evaluation demonstrated that several extracts, particularly selected extracts from G. angustifolia, G. incana, and G. weberbaueri, markedly inhibited NO production in LPS-stimulated RAW 264.7 macrophages without exhibiting cytotoxicity at the tested concentrations. Integration of metabolomic and bioactivity datasets through chemometric analysis identified flavonoid glycosides as the metabolite class showing the strongest positive association with the observed anti-inflammatory activity, highlighting these metabolites as promising candidates for future isolation and biological validation. These findings provide new insights into the valorization of Guadua leaves as a sustainable source of bioactive compounds.



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Sciforum-207198: Metabolomic characterisation of the testis in Lysosomal Acid Lipase–deficient mice highlights age-dependent changes in energy- and lipid-associated metabolites

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Metabolomic regulation is central to spermatogenesis, particularly due to metabolic support from Sertoli cells (SCs). Lysosomal acid lipase (LAL), encoded by the lipase A (LIPA) gene, participates in lysosomal lipid processing and may influence testicular metabolic homeostasis. This study explored genotype- and age-dependent testicular metabolomic alterations associated with LAL deficiency.

Testicular tissue from Lipa$^{-/-}$, Lipa$^{+/-}$, and wild-type mice was collected at 21, 70, and 150 days of age (n = 5–6/group/timepoint). Metabolomic profiling was performed using ^{1}H-NMR spectroscopy. Metabolite concentrations were normalized to tissue weight and auto-scaled prior to multivariate analysis. PCA by PERMANOVA with 999 permutations and sparse PLS-DA (5 components, 10 variables/component; performance evaluated using the platform's performance module) were conducted in MetaboAnalyst 6.0. Differential metabolite levels were assessed using ordinary one-way ANOVA with uncorrected Fisher's LSD for multiple comparisons in GraphPad Prism 10.3.1 and are reported as fold variation to control (wild-type) (mean ± SEM).

Genotype-dependent metabolic divergence was most pronounced at 21 days. Compared with wild-type, Lipa$^{-/-}$ testes exhibited increased glycerol (1.42 ± 0.18-fold; p = 0.04), glycine (1.59 ± 0.27-fold; p = 0.008), succinate (1.68 ± 0.22-fold; p = 0.005), glutamate (1.56 ± 1.9-fold; p = 0.02), and acetate (1.98 ± 0.23-fold; p = 0.03). Lipa$^{+/-}$ mice showed reduced succinate (0.53 ± 0.05-fold; p = 0.04), while taurine, succinate, and glutamate differed between heterozygotes and knockouts. At 150 days, Lipa$^{-/-}$ mice showed reduced glycine and increased acetate, ethanolamine, and alanine; Lipa$^{+/-}$ mice displayed elevated ethanolamine compared with controls and lower acetate and alanine than Lipa$^{-/-}$ mice. Pathway analysis implicated pyruvate metabolism, glycolysis, and glycerophospholipid metabolism.

LAL deficiency is associated with sustained, genotype-dependent testicular metabolomic alterations involving energy-, amino-acid-, and lipid-related pathways. These findings support altered testicular metabolic homeostasis and warrant functional studies of lysosomal lipid handling and SC-germ-cell metabolic interactions.



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