Shedding Light on the Dark Metabolome and Its Clinical Potential

A Symposium on Clinical Metabolomics, Lipidomics, and Metabolite Discovery

20–21 May 2026

Losby Gods, Oslo, Norway

Organised by

Section for Metabolomics and Lipidomics (MOL)

Oslo University Hospital

MOL | Section for MetabolOmics and Lipidomics
Department of Medical Biochemistry
OSLO UNIVERSITY HOSPITAL

Core Facility for Global Metabolomics and Lipidomics

University of Oslo

Core Facility for Global Metabolomics and Lipidomics
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Welcome

Dear Colleagues and Friends,

Some meetings are planned meticulously, years in advance, with timelines and committees and colour-coded spreadsheets. This one grew differently, out of chance encounters, shared curiosity, and the simple realisation that the right people were already within reach of each other. A few conversations over coffee, a spontaneous "wouldn't it be wonderful if...", and here we are. Serendipity, it turns out, is an excellent conference organiser.

Welcome to Losby Gods.

We are delighted to bring together clinicians, researchers, and analytical scientists from across Europe to explore one of the most exciting frontiers in modern biology: the dark metabolome and its clinical potential. The questions that unite us are big ones. What are we still missing in the metabolome? How do we move from discovery to clinical impact? What does the unexplored chemical space of the human body hold in store for medicine?

Over the next two days, we hope you will encounter not only bold and inspiring science, but also the kind of unexpected connections that only happen when curious people share good food, fresh air, and an honest conversation around the table. We believe this meeting will be quite unlike any other and, we hope, truly unforgettable.

We are deeply grateful to every speaker and attendee who made the journey here. Your presence and your science are what make this possible.

With warmth and great excitement,

Katja Benedikte Prestø Elgstøen
and the OUS MOL team

Scientific Programme

Day 1 — Wednesday, 20 May 2026

Time	Programme
8:00 – 9:30	Arrival at Losby Gods, registration and coffee
9:30 – 9:45	Welcome and opening words *Katja Benedikte Prestø Elgstøen and the OUS MOL team*
9:45 – 10:30	Invited Speaker 1 ★ **Moving the masses: travelling from small-scale untargeted metabolomics to large-scale biomedical metabolomics** *Warwick (Rick) Dunn — University of Liverpool, UK*
10:30 – 10:45	Discussion
10:45 – 11:00	Coffee break
Session 1: Clinical Metabolomics	
11:00 – 12:00	**Our approach in global metabolomics and lipidomics for clinical routine applications** *Katja Benedikte Prestø Elgstøen and the OUS-MOL team*
12:00 – 13:30	Lunch and a refreshing walk
13:30 – 14:15	Invited Speaker 2 ★ **The need for MS/MS and retention time libraries in semi-targeted clinical metabolomics** *Catherine Winder — University of Liverpool, UK*
14:15 – 14:30	Discussion
Session 2: Metabolomics in Microbiome Research	
14:30 – 15:30	**Mapping gut microbial impact on a disease of the gut-liver axis** *Peder Rustøen Braadland — Norwegian PSC Research Center, Oslo, Norway* **Bacterial-Derived Metabolites in the Bone Marrow Microenvironment are Associated with Disease Characteristics and Treatment Response in Multiple Myeloma** *Pegah Abdollahi — Oslo University Hospital, Oslo, Norway*
15:30 – 16:00	Break for check-in at the hotel and coffee break
16:00 – 16:45	Invited Speaker 3 ★ **Shots in the dark: Bottom-up pathway discovery using untargeted metabolomics** *Robert Jansen — Radboud University, Netherlands*
16:45 – 17:00	Discussion
17:00 – 19:30	Social Programme
20:00 – 22:00	Dinner

Day 2 — Thursday, 21 May 2026

Time	Programme
Session 3: New Technologies in Metabolomics	
9:00 – 9:50	**Multiplexed tracer metabolomics for mass spectrometric metabolic phenotyping of cells and tissues** *Marcel Kwiatkowski — University of Bergen, Norway* **Expanding metabolome coverage in complex matrices on the Orbitrap Excedion Pro Mass Spectrometer** *Michał Kaczmarek — Thermo Fisher Scientific, Bremen, Germany*
9:50 – 10:00	Discussion
10:00 – 10:30	Coffee break and check out
Session 4: Data Processing and Statistics	
10:30 – 11:45	Invited Speaker 4 ★ **Multi-omics of Endometriosis: Navigating the Data Processing Jungle** *Lukáš Najdekr — Palacký University Olomouc, Czech Republic* **Untargeted metabolomics reveals widespread immediate metabolomic response during ketogenic diet treatment in adults with drug-resistant epilepsy** *Kristina Gervin — Oslo University Hospital, Oslo, Norway*
11:45 – 12:00	Discussion
12:00 – 13:30	Lunch and a refreshing walk
Session 5: Roundtable Discussion	
13:30 – 14:30	**Metabolomics Education, Outreach, and the Challenge of Bringing the Field to the Clinic**
14:30 – 14:45	Coffee break
14:45 – 15:30	Invited Speaker 5 ★ **From Untargeted Discovery to Accurate Quantification in Clinical Metabolomics** *Coral Barbas — CEMBIO, Universidad CEU San Pablo, Spain*
15:30 – 15:45	Discussion
15:45 – 16:00	Closing words *Katja Benedikte Prestø Elgstøen and the OUS MOL team*

Oral Presentation Abstracts

Abstracts are presented below in two groups: invited speakers first (IS-01 to IS-05), followed by contributed oral presentations (O-01 to O-07), in order of appearance on the programme.

Invited Speaker Abstracts

IS-01 ★ Invited Speaker

Moving the masses: travelling from small-scale untargeted metabolomics to large-scale biomedical metabolomics

Warwick (Rick) Dunn

University of Liverpool, Centre for Metabolomics Research / Biochemistry, Cell and Systems Biology, UK

Wednesday, 20 May 2026 | 9:45 – 10:30

The origins of metabolomics in the late 1990s provided new technologies to allow the reporting of relative amounts for hundreds of metabolites and their subsequent statistical analysis and chemical structure elucidation in discovery/hypothesis-generating biological studies. In the subsequent 25 years both technologies and our knowledge of metabolome compositions have advanced and has allowed us to move towards more targeted studies of hundreds of metabolites where concentrations for some/all metabolites can be reported. These advances allow us to move from laboratory towards true large-scale clinical studies. In this presentation I will discuss advances which allow us to move towards large-scale clinical applications including metabolome annotation, quantitative analysis and QC procedures. I will also highlight the use of clinical metabolomics in the study of blood cancers.

IS-02 ★ Invited Speaker

The need for MS/MS and retention time libraries in semi-targeted clinical metabolomics

Catherine Winder

University of Liverpool, Biochemistry, Cell and Systems Biology, UK

Wednesday, 20 May 2026 | 13:30 – 14:15

The identification of metabolites in untargeted metabolomics studies requires the matching of experimental data (MS1, MS/MS fragmentation and chromatographic retention time) to these data in metabolite libraries. MS/MS data is available in mass spectral libraries and collected at single collision energies that are transferable between laboratories. In contrast, the data in retention time libraries are collected using specific experimental conditions that are not transferable between laboratories applying different assays. Metabolite libraries are constructed with data acquired for authentic metabolite standards, and the metabolome coverage varies and is often limited between libraries. In this presentation, I will discuss the experimental and computational approaches we are applying to increase our ability to routinely identify metabolites in untargeted and semi-targeted clinical metabolomics studies. This will include large-scale library construction and retention time mapping.

IS-03 ★ Invited Speaker

Shots in the dark: Bottom-up pathway discovery using untargeted metabolomics

Robert Jansen

Radboud University, Department of Microbiology, the Netherlands

Wednesday, 20 May 2026 | 16:00 – 16:45

Untargeted metabolomics provides a rich but unfiltered view of the dark metabolome. Translation of thousands of unfiltered analytical features to confirmed metabolites and their biochemical pathways, let alone function, remains challenging. This presentation covers historic and ongoing examples of bottom-up pathway discovery using untargeted metabolomics. We first look back at the discovery of N-lactoyl amino acids and their biosynthetic pathway in humans but then focus on Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis. One rich and untapped source of potential new TB drug targets is the sizeable part of the Mtb genome that is uncharacterized. To discover new species-specific enzymes and metabolic pathways involved in TB pathogenesis, we applied a bottom-up approach aimed at identifying new metabolites and linking them to their biosynthetic enzyme. To prioritize metabolites likely involved in pathogenesis, we performed untargeted metabolic profiling on pathogenic and non-pathogenic Mycobacterium species under various physiologically relevant stresses. Using molecular networking, we identified a group of previously uncharacterized, but chemically related, metabolites that primarily accumulate in Mtb exposed to hypoxia or nitric oxide. Structural elucidation by NMR identified the most abundant member of the family as 6-GABA-trehalose (6GT), which was confirmed using a chemically synthesized standard. 6GT has never been described before but accumulates within minutes after stress exposure and reaches high mM intracellular levels in vitro. In a more clinically relevant infection model with primary human macrophages, 6GT is formed in an interferon gamma-dependent manner. We found that 6-GABA-trehalose is formed from GABA and trehalose by an ATP-dependent enzyme that we identified as the uncharacterized "carboxylase" Rv1722. In line with our untargeted metabolomics data, the gene encoding Rv1722 is only present in pathogenic mycobacteria. The function of 6GT remains unknown.

IS-04 ★ Invited Speaker

Multi-omics of Endometriosis: Navigating the Data Processing Jungle

Lukáš Najdekr

Institute of Molecular and Translational Medicine, Palacký University, Olomouc, Czech Republic

Thursday, 21 May 2026 | 10:30 – 11:45

Endometriosis is a chronic estrogen-dependent inflammatory disease characterised by the presence of endometrial-like tissue outside the uterus. Affecting ~10% of reproductive-age women, diagnosis is frequently delayed due to nonspecific symptoms and the lack of reliable biomarkers. In this study, we applied untargeted metabolomics, lipidomics, and proteomics to identify plasma molecular signatures associated with endometriosis. Plasma samples from patients (Grades I–IV), suspected cases, and matched controls were analysed using extraction protocols optimised for metabolite and lipid profiling, followed by high-resolution LC-MS/MS in positive and negative ion modes. Data preprocessing included peak detection, QC-based signal correction (QC-RSC), and statistical filtering using the PySPRESSO pipeline. Multivariate analyses (PCA, PLS-DA) revealed differences between controls and diagnosed cases. Multi-Omics Factor Analysis (MOFA) identified latent factors associated with disease class. Structural elucidation of selected lipids was performed using ultraviolet photodissociation (UVPD) on an Orbitrap Ascend, enabling precise localisation of double bond positions. Lipids such as PC(16:0_20:5) showed differential abundance and fragmentation patterns between groups. These results highlight the potential of plasma multi-omics for biomarker discovery in endometriosis and demonstrate the utility of UVPD for structural lipidomics.

IS-05 ★ Invited Speaker

From Untargeted Discovery to Accurate Quantification in Clinical Metabolomics

Coral Barbas

Centre of Metabolomics and Bioanalysis (CEMBIO), Universidad CEU San Pablo, Madrid, Spain

Thursday, 21 May 2026 | 14:45 – 15:30

Untargeted lipidomics provides a broad view of metabolic alterations and enables the identification of disease-associated signatures. Using this approach, we identified early disruptions in lipid metabolism in pediatric obesity, revealing metabolic alterations linked to inflammation and metabolic risk. To facilitate compound annotation and improve comparability across studies, we developed a semi-targeted strategy based on a curated library of metabolites characterized in certified reference plasma. This approach supports more robust identification and harmonization in clinical metabolomics workflows. For metabolite families present at very low concentrations and with high structural complexity, targeted strategies are essential. Oxylipins represent a paradigmatic example, as their accurate quantification requires selective analytical methods capable of resolving complex isomeric mixtures and detecting low-abundance lipid mediators. Together, these complementary strategies illustrate how untargeted discovery, semi-targeted annotation, and targeted quantification can be integrated to advance lipidomics in clinical research.

Contributed Oral Presentations

O-01

Our approach in global metabolomics and lipidomics for clinical routine applications

Katja Benedikte Prestø Elgstøen and the OUS-MOL team

Oslo University Hospital, Section for Metabolomics and Lipidomics (MOL), Norway

Wednesday, 20 May 2026 | 11:00 – 12:00

Global untargeted metabolomics and lipidomics have long been established as powerful tools in research settings, yet their translation into clinical routine practice remains a work in progress. At the Section for MetabolOmics and Lipidomics (MOL) at Oslo University Hospital, we operate at the intersection of these two worlds: applying discovery-grade platforms within the framework and accountability of a hospital diagnostic laboratory.

In this talk, we present our current approach to clinical metabolomics and lipidomics, including the workflows, platforms, and quality systems we have built to support routine analytical delivery. We share concrete use cases and clinical examples where global profiling has contributed meaningful insight, illustrating both the promise and the complexity of working with metabolomics data in a clinical context. We will introduce the concept of one-sample approach and our goal to establish reference metabolomes.

We also address the considerable challenges that remain. Hospital laboratory practice demands a level of robustness, reproducibility, and regulatory compliance that research environments rarely require. Standardisation of pre-analytical variables, inter-laboratory harmonisation, and the lack of universally accepted reference ranges are among the key bottlenecks limiting broader clinical implementation. Furthermore, the interpretive gap between a metabolomics result and a clinically actionable conclusion is one that cannot be closed by analytical quality alone.

We hope this session opens a broad conversation about where the field stands today, what it will take to move forward, and what clinicians and laboratory specialists need from the metabolomics community to make that happen.

O-02

Mapping gut microbial impact on a disease of the gut-liver axis

Peder Rustøen Braadland

Norwegian PSC Research Center, Norway

Wednesday, 20 May 2026 | 14:30 – 15:30

The liver is continuously exposed to portal blood transported from the intestine. Primary sclerosing cholangitis (PSC) is a chronic inflammatory disease of the liver and bile ducts. Most patients will eventually need a liver transplant. Disease recurrence (rPSC) is common, however, and suggests that extra-hepatic factors are involved in its etiology. PSC typically co-occurs with inflammatory bowel disease and loss of gut microbial diversity, and surgical removal of the colon is associated with improved outcomes. We therefore hypothesized that these extra-hepatic factors are gut microbial byproducts. We performed untargeted LC-MS/MS (Metabolon) on plasma from >200 people with PSC before and after liver transplantation and 33 healthy controls, integrating these data with metabolomic profiles of germ-free and conventionally raised mice, as well as public databases of microbiota-host co-metabolites. We find that PSC entails large alterations in the circulating metabolome, in part driven by depletion of microbial metabolites, which was particularly pronounced in patients lacking a colon. While most metabolomic changes reversed after liver transplantation, microbial metabolites remained persistently depleted. As opposed to the majority of microbial metabolites, imidazole propionate was increased in PSC. Experimental validation showed that imidazole propionate induces bile duct injury and worsens PSC, illustrating feasibility of our pipeline and the gut-liver axis in this orphan disease.

O-03

Bacterial-Derived Metabolites in the Bone Marrow Microenvironment are Associated with Disease Characteristics and Treatment Response in Multiple Myeloma

Pegah Abdollahi

Oslo University Hospital, Oslo Myeloma Center, Norway

Wednesday, 20 May 2026 | 14:30 – 15:30

Introduction: Multiple myeloma (MM) is a plasma cell malignancy driven by interactions within the bone marrow (BM) microenvironment. Despite advances in therapy, MM remains incurable. Minimal residual disease (MRD) negativity is linked to improved outcomes, but determinants of treatment response remain unclear. Microbiota-derived metabolites have emerged as potential modulators of cancer biology. We investigated their presence in BM and their potential association with disease characteristics and outcomes. Methods: BM and peripheral blood plasma samples were collected from 382 newly diagnosed MM patients in the REMNANT phase 2/3 trial. MRD status was assessed after first-line therapy (EuroFlow, sensitivity 10^{-5}). Targeted metabolomics quantified 20 bacterial-derived metabolites in BM plasma (n=76) and matched blood samples (n=10). Associations with MRD, progression-free survival (PFS), and clinical characteristics were analyzed using adjusted multivariable models. Results: Most metabolites showed comparable levels in BM and blood. Indole-3-propionic acid (IPA) was significantly higher in MRD-positive patients. Phenylacetylglutamine and betaine showed borderline associations with PFS. Several metabolites including imidazole propionate, indole derivatives, and choline-derived metabolites were associated with renal impairment. Formate and butyrate correlated with bone disease. Additionally, indoxyl sulfate and dimethylglycine were positively associated with higher clonal plasma cell burden. Conclusion: Bacterial metabolites were detectable in the BM microenvironment and showed associations with MRD and disease characteristics, supporting their potential as biomarkers of treatment response. However, these preliminary findings should be interpreted with caution, as some metabolites, including formate, can arise from both gut microbial and host metabolism.

O-04

Multiplexed tracer metabolomics for mass spectrometric metabolic phenotyping of cells and tissues

Marcel Kwiatkowski

University of Bergen, Department of Biomedicine, Norway

Thursday, 21 May 2026 | 9:00 – 9:50

Biological systems maintain homeostasis, with cellular metabolism playing a central regulatory role. Metabolic alterations are hallmarks of numerous pathological conditions, including cancer, cardiovascular and metabolic diseases, inflammation, and neurological disorders. Metabolic phenotyping is therefore essential for dissecting metabolic pathways. However, widely used approaches based on oxygen consumption and extracellular acidification provide only indirect readouts and require metabolic inhibitors, introducing additional perturbations. To address these limitations, we developed an MS-based multiplexed metabolic phenotyping (M3P) approach. This tracer metabolomics approach combines stable isotope-labelled glucose and glutamine with a rapid RP-OT-MS workflow to quantify label incorporation into key metabolites of aerobic and anaerobic glycolysis, the TCA cycle, and glutaminolysis. The method provides high sensitivity (LLOQ ≤ 0.4 µM), accuracy (MAPE ≤ 6%), and reproducibility (CV = 8%) for pyruvate, lactate, α-ketoglutarate, citrate, succinate, and short-chain acyl-CoAs including acetyl-CoA. We demonstrate that M3P enables robust metabolic phenotyping of cell cultures and tissue slices. Using this approach, we show that AKT inhibition decreases glycolysis while enhancing glutaminolysis, and we characterize the metabolic consequences of neuron depolarization on glycolytic and mitochondrial pathways.

O-05

Expanding metabolome coverage in complex matrices on the Orbitrap Excedion Pro Mass Spectrometer

Michał Kaczmarek

Thermo Fisher Scientific, Metabolomics, Germany

Thursday, 21 May 2026 | 9:00 – 9:50

Untargeted metabolomics in complex matrices is often limited by insufficient sensitivity, restricted intra-scan dynamic range, and unintended in-source fragmentation, which can obscure low-abundance metabolites and complicate annotation. The Thermo Fisher Scientific Orbitrap Excedion Pro mass spectrometer introduces developments within an end-to-end LC–HRAM-MS workflow designed to expand metabolome coverage and improve annotation confidence. The platform incorporates an electrodynamic ion funnel engineered for high ion transmission under mild transfer conditions, reducing unintended MS1 fragmentation of labile metabolites. In a plant extract example, the phenylalanine fragment-to-precursor ratio in tea decreased from 51% on an Orbitrap Exploris 480 MS to 35% on the Orbitrap Excedion Pro, supporting cleaner precursor-based annotation. To improve low-abundance feature detection, the Orbitrap enhanced Dynamic Range (eDR) scan mode applies intelligent MS1 multiplexing with optimized injection times, dividing the mass range into two alternating Orbitrap MS1 subscans. In chamomile tea extracts, eDR increased reproducibly detected features and ChemSpider-annotated compounds 1.8-fold. Combined with AcquireX DeepScan DDA, the workflow increased the number of MS2 spectra and mzCloud annotations, with similar benefits observed in human plasma. Data processing was supported by Compound Discoverer 3.5 and mzCloud 2.0 database matching.

O-06

Untargeted metabolomics reveals widespread immediate metabolomic response during ketogenic diet treatment in adults with drug-resistant epilepsy

Kristina Gervin

Oslo University Hospital, Department of Research and Innovation, Norway

Thursday, 21 May 2026 | 10:30 – 11:45

Background: The ketogenic diet (KD) is increasingly used as an adjunctive therapy for drug-resistant epilepsy and triggers a shift from carbohydrate to lipid-derived energy metabolism. A comprehensive characterisation of the system-wide metabolomic response to KD is still lacking, and interpretation is further limited in untargeted LC-MS data by the large proportion of unannotated signals ("dark metabolome"). Methods: We performed longitudinal untargeted LC-MS metabolomics with repeated sampling at baseline, week 4, and week 12 during a KD intervention in patients (n=64) with treatment-refractory epilepsy. Global metabolome shifts were assessed by principle component analyses (PCA) and by quantifying systemic remodelling as the mean absolute within-individual log10 change across all detected features between timepoints. Feature-level changes across time contrasts were evaluated using paired t-tests on log10 intensities with Benjamini-Hochberg false discovery rate (FDR) correction, and effect sizes were summarised as log10 fold changes. To improve interpretability beyond single-feature results, we applied co-variation clustering (WGCNA modules) and within-module correlation networks anchored by Level 1 and 2 metabolites, integrating database-based candidate annotation and network-guided prioritisation of unannotated features for targeted MS/MS follow-up. Results: KD treatment was associated with a clear global metabolic shift across timepoints, with the largest overall change observed during KD initiation (baseline to week 4) and smaller additional change between weeks 4 and 12. At the feature level, baseline comparisons yielded hundreds of significant changes in both ion modes, whereas far fewer features changed between week 4 and 12, indicating a pronounced early response followed by relative stabilisation. Module- and network-level analyses identified coordinated response structures anchored by Level 1/2 metabolites, providing preliminary biochemical context consistent with remodelling in amino-acid-linked pathways, acylcarnitine-associated fatty acid transport/beta-oxidation, and indole/tryptophan-related metabolism. Conclusions: In patients with drug-resistant epilepsy, ketogenic diet intervention induced a rapid and widespread metabolomic shift that largely stabilised after initiation and persisted to 12 weeks. By integrating global remodelling summaries with network-guided anchoring, we organised several hundred signals into coherent response modules and prioritised unannotated features for MS/MS confirmation, improving biological interpretability of the KD response.

Roundtable Discussion

RD-01

Metabolomics Education, Outreach, and the Challenge of Bringing the Field to the Clinic

Thursday, 21 May 2026 | 13:30 – 14:30

Metabolomics and lipidomics have matured enormously as scientific disciplines, yet their presence in formal education curricula, from universities to hospital training programmes, remains uneven and often insufficient. As the field moves closer to clinical application, the gap between what practitioners need to know and what they are actually being taught becomes increasingly consequential.

This session brings together educators, clinicians, and laboratory specialists for an open panel discussion on the state of metabolomics and lipidomics education across Europe. Where does the field currently feature in university programmes, and how consistent is that coverage between countries and institutions? What does a clinician, a laboratory specialist, or a medical biochemist actually need to understand about metabolomics, and are we giving them the tools to understand it?

Beyond formal teaching, we also want to explore the broader challenge of promotion and popularisation: how do we build awareness and enthusiasm among medical staff who may never run a mass spectrometer but who will increasingly encounter metabolomics results in a clinical report? What works, what does not, and what can we learn from each other's experiences?

The panel will open with brief perspectives from the speakers before opening the floor to the audience. We encourage everyone in the room to contribute, whether you have taught a course, sat through one, tried to explain a volcano plot to a physician, or simply wondered why this is not talked about more. This is a session for honest reflection and, we hope, a few good ideas.