nature communications

Perspective

https://doi.org/10.1038/s41467-026-73797-4

A lipidomics roadmap: from basic research to societal challenges

Received: 18 August 2025

Accepted: 21 May 2026

A list of authors and their affiliations appears at the end of the paper

Lipidomics, a rapidly evolving discipline at the interface of biology and analytical chemistry, seeks to comprehensively characterize the lipid composition of biological systems. Driven by advances in mass spectrometry, chromatography and computational analysis, lipidomics has enabled the high-resolution mapping of lipid networks and their functional dynamics across molecular, cellular and organismal scales. In biomedical research, lipidomics is emerging as a powerful platform for biomarker discovery, enabling early diagnosis, prognosis, and therapeutic monitoring of cancer, metabolic, and neurodegenerative diseases. The field is also reshaping drug discovery by uncovering lipid-mediated pathways, identifying novel therapeutic targets, and refining assessments of drug efficacy and safety. Beyond medicine, lipidomic analyses are redefining food and nutrition science by elucidating how dietary lipids influence metabolic health and disease risk. In parallel, environmental and ecological lipidomics are emerging as powerful frameworks for assessing ecosystem health, tracking the impact of pollutants and exploring the biological consequences of climate change. Such approaches are also informing the discovery of sustainable lipid resources and the development of novel biotechnological and agricultural innovations. With its rapidly expanding analytical repertoire and cross-disciplinary relevance, lipidomics is poised to make substantial contributions to both fundamental biology and applied science. This Perspective aims to synthesise the current state of the field, delineate major analytical and conceptual challenges, and outline future directions for translating lipidomic knowledge into tangible societal and environmental benefits.

Lipids are a diverse group of small, amphiphilic or hydrophobic molecules with a wide range of chemical structures that underlie their many biological functions and activities. Once considered merely structural components of biological membranes and reservoirs for energy storage, lipids are now at the forefront of modern research. They are recognized for their critical roles in signal transduction, regulation of electrochemical gradients, central involvement in metabolic networks, and in mediating communication between organelles and cells[1,2]. Because of their direct involvement in essential biological processes, disruptions in lipid levels or failures in lipid quality control, at the cellular, tissue, or whole-organism level, are increasingly linked to numerous human diseases and the aging process[3–5].

Lipid metabolism has been a focus of scientific inquiry since the early 20th century. In recent decades, however, lipid research has undergone a transformative evolution as advances in analytical technologies now enable the study of intact lipids at an "omics" scale[6]. Modern lipidome research is opening new dimensions in both basic and applied biomedical research, enabled by advances in lipidomics technology (Box 1). In this Perspective, we aim to provide a comprehensive overview of recent advances in lipidomics, address current

e-mail: maria.fedorova@tu-dresden.de; mrd@ua.pt

BOX 1

Lipidome and lipidomics

The terms “lipidome”[179] and “lipidomics”[180] were first introduced between 2001 and 2003. The lipidome represents the complete set of lipids in a given biological system, while lipidomics refers to the comprehensive, large-scale analysis of cellular lipids, encompassing their structural diversity, spatial distribution, functional roles, involvement in metabolic networks, and interactions with other biomolecules. The emergence of lipidomics marked a pivotal shift toward high-throughput, systems-level lipid analysis, enabled by advanced analytical technologies such as mass spectrometry (MS) often coupled with separation techniques. Since 2003, lipidomics has undergone transformative development, both in terms of the analytical and computational tools now available[7,181], and in the breadth of its applications, ranging from clinical translation to ecosystem health[124,147,182–184].

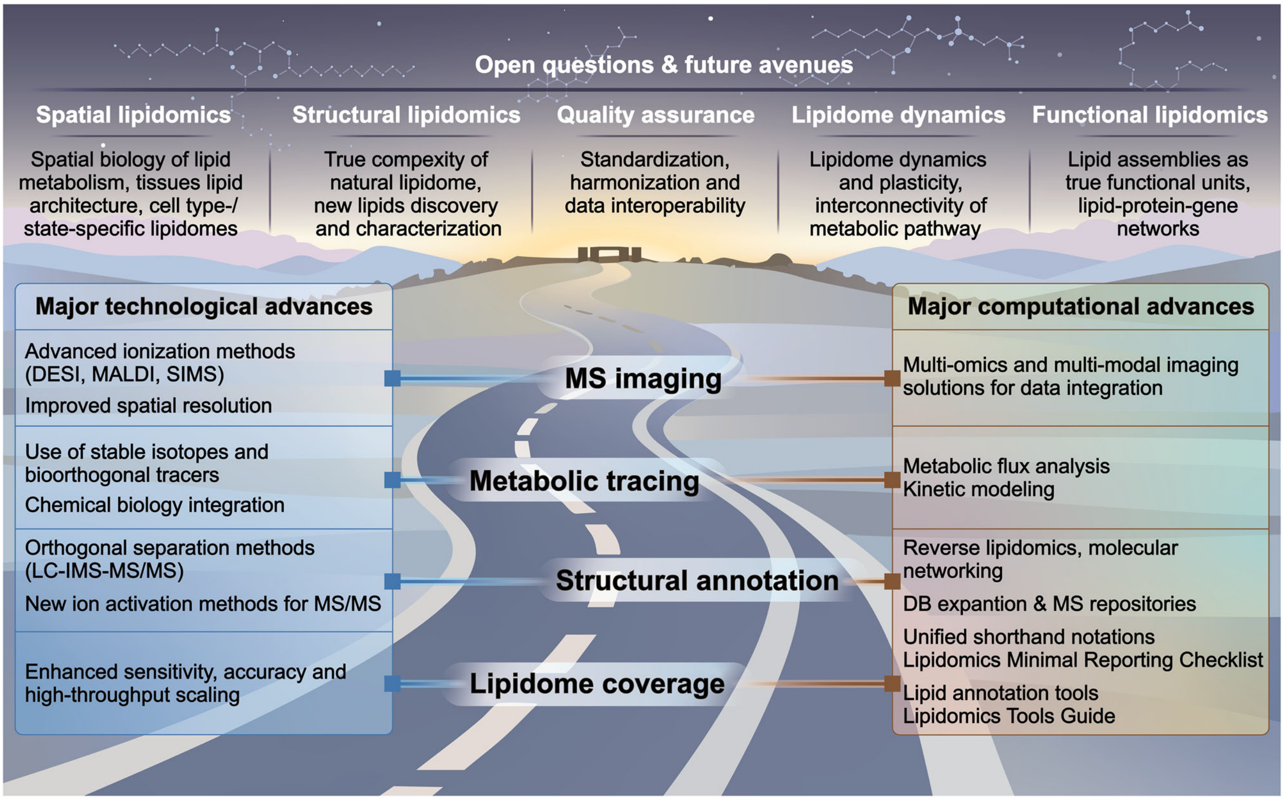

Fig. 1 | The lipidomics roadmap. An overview of key technological milestones that have driven the emergence and evolution of the lipidomics field. The figure highlights parallel advancements in analytical platforms and computational data processing, as well as anticipated future directions poised to shape the next phase of lipid research. DB – database; DESI – desorption electrospray ionization; IMS – ion mobility spectrometry; LC – liquid chromatography; MALDI – matrix assisted laser desorption ionization; MS – mass spectrometry; MSI – mass spectrometry imaging; SIMS – secondary ion mass spectrometry.

challenges, and outline future directions for the field (Fig. 1). Our primary goal is not only to summarize the current state of the art, but more importantly, to highlight emerging technologies, potential applications, and key challenges across a wide range of disciplines, from basic biological research to translational science in healthcare, nutrition, as well as ecology and environmental sciences.

Technological developments in lipidomics: advances and challenges

Technological developments in bioanalytical chemistry and MS instrumentation have led to significant advances in lipidomics[7] (Fig. 1, Box 2). Improved sensitivity (4–5 orders of magnitude since the 1980s[8,9]) and mass accuracy (sub-ppm) of modern high-resolution analytical platforms have markedly expanded the detectable breadth of lipid subclasses. Compared to the dozens of lipids typically reported in the early 2000s, current lipidomics workflows now routinely allow the annotation of several hundred lipid molecular species[10,11] and have facilitated the characterization of previously unrecognized or poorly characterized classes (e.g., maradolipids[12], ecdysteroids[13], or endocannabinoid-related N-acylamidated amino acids[14]). In particular, the hyphenation of complementary separation modalities has increased the overall peak capacity of analytical platforms. For example, the integration of liquid chromatography (LC), which separates analytes based on polarity and/or hydrophobicity, with ion mobility spectrometry (IMS), which resolves ions according to mass-to-charge ratio and gas-phase conformation, with mass spectrometry (MS) has substantially expanded the detectable coverage of complex lipidomes[15]. In parallel, the development of alternative ion activation modalities has enabled deeper structural annotation and laid the foundation for structural lipidomics. Current methods for resolving double-bond positional isomers rely either on chemical derivatization strategies (for example, the Paternò–Büchi reaction) or on alternative

BOX 2

Major technological advances in modern lipidomics

- Marked improvements in the sensitivity, resolution and mass accuracy of modern mass spectrometry platforms.
- Quantitative lipidomics enabled by the systematic use of isotopically labelled internal standards.
- Hyphenation of separation strategies that combine liquid chromatography (LC), ion mobility spectrometry (IMS) and MS (including MS/MS), substantially increasing molecular coverage and confidence in lipid annotation.
- Development of new ion activation methods for tandem MS (e.g., electron-induced dissociation (EID) and ultraviolet photodissociation (UVPD)), facilitating detailed structural characterization, including assignment of *sn*-positional isomers and double-bond locations.
- Expansion of mass spectrometry imaging (MSI) approaches, enabling spatially resolved lipidomics and integration with complementary omics and imaging modalities.

gas-phase fragmentation techniques, including ozone-induced dissociation (OzID), electron-induced dissociation (EID), oxygen attachment dissociation (OAD) and ultraviolet photodissociation (UVPD). These approaches enable the differentiation of isomeric lipids with respect to *sn*-position and double-bond location[16–18].

Resolving spatial organization of tissue lipidomes using MS imaging (MSI) represents another major technological breakthrough. Spatial proteomics was named the Method of the Year in 2024[19], and lipidomics applications of MSI are steadily catching up[20]. The combination of MSI with high-resolution MS, ion mobility, and various ionization methods[21–23] has enabled the construction of the first spatially resolved maps of different tissues and organs[24] and revealed the molecular heterogeneity of cell populations[25]. Although quantitative MSI remains challenging, progress has been made through the development and application of suitable mixtures of internal standards[26]. Moreover, integrating MSI with complementary label-based and label-free techniques, including immunofluorescence mapping of cellular identities[27], nanoscale spectroscopic methods such as Raman spectroscopy[28] and multi-omics approaches[29], is opening new opportunities for systems-level analyses of lipid biology[30].

Next, significant progress has been made in extending lipidomics toward the analysis of lipidome dynamics, driven by advances in chemical biology[31] and bioorthogonal tracing methods[32–34], together with the broader adoption of metabolic flux analysis[35]. When integrated with classical biochemical approaches, these strategies provide a more detailed view of lipid metabolism and function. The combination of complementary dimensions, such as temporal dynamics from metabolic tracing and spatial localization from imaging lipidomics, will enable lipidomics to move beyond static inventories of lipid species toward a systems-level understanding of lipid biology within living tissues and their microenvironments.

Although advanced lipidomics workflows described above remain areas of specialization, conventional solutions based on the application of LC-MS/MS or shotgun lipidomics have become widely accessible to researchers through platforms built by individual laboratories or core institutional facilities. The increasing “democratization” of lipidomics, driven by broader access to instrumentation, a growing pool of trained operators and decreasing analytical costs, has made the technology accessible to a wide range of researchers, supporting applications from biomarker discovery to detailed investigations of lipid metabolism and biology. The widespread adoption of lipidomics has also generated large datasets, facilitating deposition in public repositories, enabling cross-study reuse and integration, and supporting the development of lipidomics atlases that define organ-specific lipid signatures[36–41].

Despite the increasing accessibility and adoption of lipidomics, major challenges remain in the accuracy of lipidome annotation and quantification[42,43]. Although advances in structural lipidomics enable deeper identification, overall annotation confidence remains limited and structural over-reporting still occurs[44,45]. Quantitative lipidomics is further constrained by the lack of harmonized workflows and standardized guidelines addressing factors such as ionization adducts, in-source fragmentation and matrix effects[46,47]. In addition, the limited availability of stable isotope-labelled internal standards and certified reference materials remains a major barrier to accurate absolute quantification and inter-laboratory comparability. Community efforts have begun to address these issues. Early initiatives by LIPID MAPS brought together researchers and standard manufacturers to expand the availability of lipid standards. More recently, the adoption of unified shorthand notation following LIPID MAPS classification, the Lipidomics Minimal Reporting Checklist introduced by the Lipidomics Standards Initiative, and reporting standards from the Metabolomics Standards Initiative and mQACC aim to establish community-wide guidelines and improve data quality and reproducibility[48–52].

Computational solutions for lipidomics: navigating the complexities of lipid data

The evolution of high-throughput instrumentation has driven the parallel development of specialized bioinformatics tools, ranging from lipid annotation to the integration of lipidomics with other omics datasets (Fig. 1, Box 3). To support users in navigating the growing ecosystem of open-source tools, the lipidomics community has also developed a centralized Lipidomics Tools Guide[53], hosted on LIPID MAPS, offering a curated overview of available resources and their applications across the lipidomics workflows. Thus, for untargeted lipidomics data, a range of approaches, including spectral library matching, rule-based annotation and hybrid methods, are now widely available[54,55]. However, metabolomics tools based on in silico fragmentation using AI and machine learning remain rarely adopted in lipidomics, as they require fully resolved structures to predict fragment ions[56,57]. In parallel with advances in experimental technologies, new tools are emerging for the annotation of double-bond positions within lipid acyl chains[54,58]. The growing application of MSI further highlights the need for automated, scalable solutions tailored to spatial lipidomics[59–63]. A similar gap exists in metabolic tracing and flux analysis, where experimental progress has outpaced the development of bioinformatics tools capable of handling complex, multi-dimensional datasets[34,64]. Yet, the large number of independently developed software tools has introduced challenges in data interoperability, as lipid identifications are often reported using different annotation criteria and formats. This issue has been partly addressed through lipid identifier conversion tools[65,66], as well as community-driven efforts led by LIPID MAPS to standardize lipid nomenclature using harmonized shorthand notation[50].

The rapid expansion of measured lipid diversity has been supported by dedicated structural databases such as the LIPID MAPS Structure Database (LMSD), SwissLipids and LipidBank[67–69]. These resources are increasingly being curated to include metadata and contextual information, transforming them from static repositories into integrative knowledge platforms. Complementing these efforts

BOX 3

Major advances in lipidomics-oriented software and computational tools

- Development and iterative refinement of lipid annotation tools enabling efficient processing of high-throughput LC-MS/MS datasets.
- Emergence of new software solutions to support advances in structural and spatial lipidomics, as well as metabolic tracing of lipid pathways.
- Establishment and expansion of comprehensive lipid structural databases.
- Broad adoption of MS data repositories for lipidomics dataset deposition, enhancing data accessibility, transparency and reuse.

are curated MS data repositories such as Metabolomics Workbench[70] and MetaboLights[71], which facilitate data reuse and cross-study comparisons by providing lipidomics datasets in standardized formats (e.g., mzML) along with associated metadata.

Despite substantial progress in analytical and computational tools, comprehensive characterization of the full diversity of lipid species in natural lipidomes remains elusive. New lipid structures continue to be discovered, underscoring the dynamic and incomplete nature of current lipidome coverage. The concept of “dark matter” in LC–MS/MS-based lipidomics reflects this gap, as only a fraction of features in untargeted datasets can currently be annotated[72]. This is partly due to ionization adducts, in-source fragments and multiple aggregation states of the same analyte[73]. However, a substantial proportion of features remains unannotated due to missing reference spectra or undefined fragmentation rules. Efforts to resolve this “dark lipidome” are accelerating, with emerging computational approaches designed to interrogate under-annotated spectral data[74,75]. Reverse metabolomics[76,77], molecular networking[78] and Mass Spectrometry Query Language (MassQL)[79] are increasingly being adapted for lipidomics to support large-scale annotation. In parallel, resources such as PartialDB, developed by LIPID MAPS and EpiLipidNET, provide curated MS/MS spectra of partially characterized lipids, enabling recognition of recurrent fragmentation patterns and supporting their prospective identification.

Clinical lipidomics: transforming metabolic health assessment

One of the most promising yet formidable frontiers for lipidomics lies in its clinical translation (Fig. 2). Given the central role of dyslipidaemia, a condition marked by abnormal lipid abundance in circulation and perturbed lipid metabolism, and altered lipid signalling in the pathogenesis and progression of a wide spectrum of metabolic[80] and degenerative diseases[81], including cancer[82], lipids hold significant potential as biomarkers for susceptibility, diagnosis, prognosis, and pharmacodynamic monitoring, as well as therapeutic targets[83,84]. Despite this promise, only a limited number of lipidomic assays have been incorporated into routine clinical practice, with FDA- and EMA-approved commercial tests or laboratory-developed tests (LDTs) remaining scarce. Notable exceptions include nuclear magnetic resonance (NMR)-based lipoprotein subclass analysis[85] and targeted MS quantification of acylcarnitines, a critical component of newborn screening programmes for inherited metabolic disorders[86]. Another LC-MS/MS-based screening application is the quantification of LPC (26:0) in dried blood spots, now included in newborn screening for X-linked adrenoleukodystrophy (X-ALD). X-ALD is a common leukodystrophy, with an estimated incidence of ~1 in 15000 births, caused by pathogenic variants in ABCD1 gene, which encodes a peroxisomal transporter required for import of very long-chain fatty acids for β-oxidation. Although affected infants are asymptomatic at birth, ~80% develop adrenocortical insufficiency before adulthood, making early detection critical for timely intervention against adrenal and neurological disease[87]. First implemented in New York State in 2013[88], X-ALD screening has since been adopted across most U.S. states, as well as in the Netherlands and Taiwan, with pilot programmes underway in Japan, Italy and China[89].

The advent of high-throughput targeted lipidomics has enabled large-scale profiling in population cohorts, underpinning two clinically significant avenues: genome-wide association studies (GWAS) of lipid traits and lipidomics-based metrics for metabolic health assessment. Recent GWAS efforts in over 1.6 million individuals of diverse ancestries have identified more than 900 genetic loci linked to classical blood lipid parameters, such as total, LDL, and HDL cholesterol, and triacylglycerols[90]. Integration of these genetic studies with MS-based lipidomics, which quantifies hundreds of circulating lipid species, has expanded understanding of the genetic architecture underlying lipid metabolism and its connections to complex diseases[91,92]. High-throughput plasma and serum lipidomics has also uncovered novel lipid biomarkers beyond the traditional clinical panel. Thus, serum ceramides have emerged as robust risk stratifiers in coronary artery disease[93,94], leading to clinical implementation of ceramide assays at institutions such as the Mayo Clinic[95]. The ceramide-based risk score CERT2, incorporating phosphatidylcholine (PC) species alongside ceramides[96], has been licensed to Quest Diagnostics for clinical assay development. More sophisticated lipidomic risk models have been proposed for primary prevention screening[97]. Recently, a plasmalogen-based score reflecting circulating 1-alkenyl-2-acyl-glycerophosphoethanolamines has been associated with reduced cardiometabolic risk and all-cause mortality, positioning it as an independent and potentially modifiable marker of metabolic health[98]. Notably, high-throughput lipidomic profiling of large cohorts has revealed pronounced sex differences in plasma lipidomes of both healthy individuals[99] and those with metabolic disorders[100,101], underscoring biological sex as a critical determinant in the pathophysiology of metabolic disorders.

The identification of novel lipid biomarkers linked to human metabolic health, together with large-scale quantitative screening, has increased interest in the clinical and commercial potential of lipidomics. A key step forward has been the shift from relative measurements to absolute lipid concentrations, providing an essential foundation for clinical translation. However, this also highlights persistent challenges in method validation, standardization and harmonization, particularly in quality assurance. Accurate absolute quantification remains difficult, especially for large lipid panels, due to the limited availability of isotopically labelled standards[102,103]. Variability in reported concentrations further underscores the need for well-characterized reference materials to ensure inter-study and inter-laboratory comparability[104]. Community-driven adoption of shared reference samples has demonstrated potential to harmonize data generated across diverse MS platforms and laboratories[105]. Recognizing this imperative, concerted efforts such as ring trials organized by the Singapore Lipidomics Incubator (SLING) and the Reference Materials and Biological Reference Ranges Interest Group of the International Lipidomics Society (ILS) have been launched. A recent

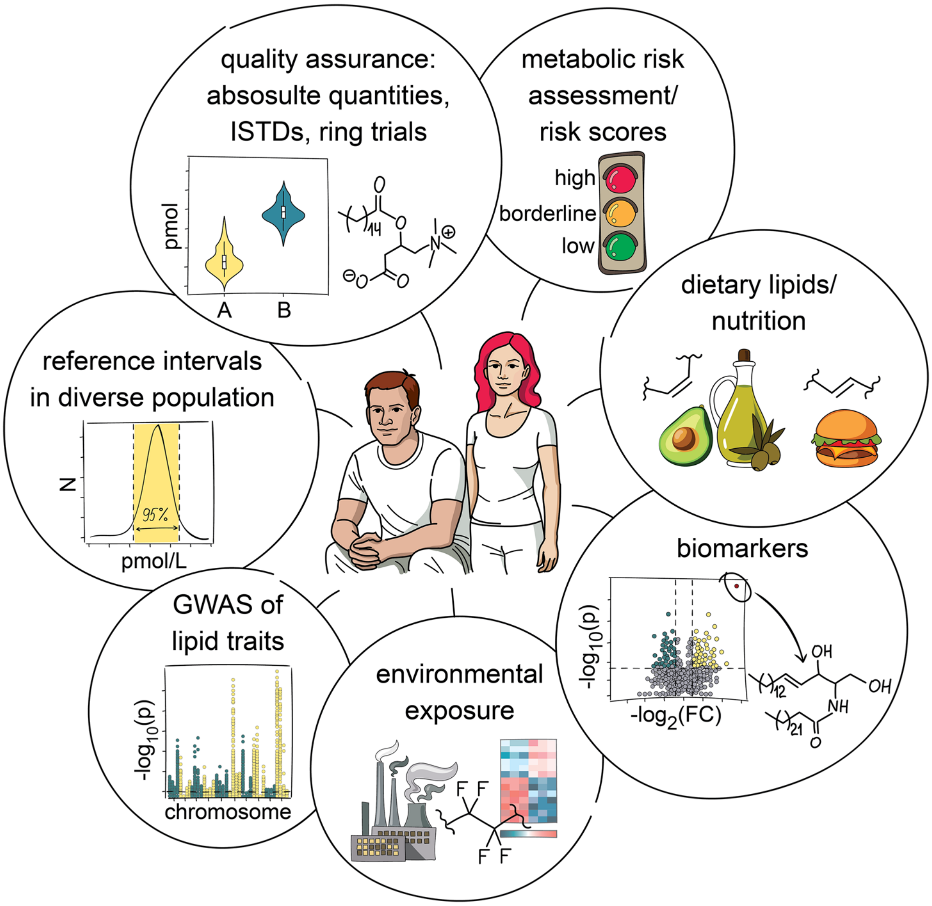

Fig. 2 | Dawn of clinical and healthcare-directed lipidomics. Key pillars supporting the translation of lipidomic workflows into clinical and public health applications. The figure illustrates the potential of lipidomics to inform diagnostic panel development, monitor exposure to environmental pollutants, guide nutritional recommendations, and uncover therapeutic targets, considering variability across sex, age, and demographic groups. GWAS - genome-wide association studies; ISTDs – internal standards.

interlaboratory study focused on quantifying four ceramides relevant to cardiovascular risk highlighted the importance of authentic labelled standards and shared reference materials[106]. Additional ring trials targeting bile acids and blood plasma lipidomes are ongoing. As quantitative reproducibility improves, lipidomics is moving towards establishing reference intervals for individual lipids and composite scores in healthy populations, a key step for clinical implementation that will require careful stratification across demographic and physiological variables. Achieving this goal will require comprehensive evaluation of reference intervals across diverse populations, including stratification by age, sex, comorbidities, diet and hormonal status.

The clinical implementation of both simple lipid panels, comprising a few species, and complex profiles encompassing hundreds of lipid molecules offers transformative potential for the diagnosis and management of inflammatory, cardiometabolic, neurodegenerative disorders, and cancer. Integrating quantitative lipidomics with advanced statistical and epidemiological modelling will enable the development of predictive frameworks expressed as risk or health scores, positioning lipids as independent and modifiable markers of metabolic health influenced by diet and lifestyle. Beyond their utility as biomarkers, lipids themselves represent promising therapeutic targets, given their central role in shaping metabolic and phenotypic responses (Box 4). Over the coming decade, clinical lipidomics is poised to expand rapidly within established healthcare pathways and the burgeoning field of precision medicine. Large-scale lipidomic data derived from population biobanks, such as the UK Biobank, FINNGEN, and NAKO, will provide unprecedented insights into the interplay of lifestyle, environment, and genetics, underpinning advances in disease prevention and personalized healthcare[107,108].

Lipidomics in human toxicology: unveiling the impact of environmental pollutants

Lipidomics has become an essential tool for investigating how environmental pollutants affect human health by interacting with the lipidome (Fig. 2). Environmental factors and toxins, including UV radiation, organic pollutants, plastics, nanoparticles, and heavy metals, contribute to the “exposome”, defined as the cumulative environmental chemical exposures an individual experiences throughout life[109]. Growing evidence suggests lipids are reliable biomarkers for assessing the toxic effects of environmental exposures. Thus, oxidized lipids (epilipids) have emerged as valuable molecular markers of senescence for monitoring both chronological skin aging and UV-induced damage[110–112]. Lipidomics has provided crucial insights into the effects of per- and polyfluoroalkyl substances (PFAS), a group of persistent pollutants of anthropogenic origin that gained popularity with the advent of Teflon but are now used in a wide range of products. PFAS exposure has been linked to inflammation and liver damage, with prenatal and early-life exposure leading to lipid profile changes associated with diseases such as type 1 diabetes[113,114]. Similarly, lipidomic analysis has proven valuable in monitoring the toxicity of microplastics and heavy metals[115,116].

Despite these advancements, studying the exposome remains challenging due to the complex and unpredictable nature of toxic mixtures, which can interact synergistically or antagonistically[117].

BOX 4

Discovery and clinical significance of an alternative fatty-acid desaturation pathway that supports tumour metabolic plasticity

Advanced structural lipidomics has enabled new insights into cancer metabolism by revealing an alternative fatty-acid desaturation pathway that supports tumour plasticity. This pathway permits certain tumours to circumvent stearoyl-CoA desaturase (SCD) by generating monounsaturated fatty acids (MUFAs), notably sapienate (16:1 ω–10), in an SCD-independent manner via fatty acid desaturase 2 (FADS2)[185]. Importantly, sapienate is both structurally and functionally distinct from its isomer palmitoleate (16:1 ω–7). In prostate cancer cell lines, LC-OzID-MS demonstrated that SCD inhibition triggers accumulation of ω–10 and ω–12 MUFAs, providing direct structural evidence for FADS2-mediated metabolic compensation[177]. Given that SCD inhibitors are being pursued as promising therapeutic agents, with some compounds, including MTI-301 already in clinical trials (e.g., NCT06911008), the ability to identify tumours capable of activating FADS2-driven MUFA synthesis will be crucial for predicting non-responders to SCD-targeted therapies. Beyond MUFAs, multiple lipid classes, including cholesterol, ceramides and plasmalogens hold potential for modulation, offering new avenues for therapeutic strategies[186].

Human exposome research is critical, as individual responses to environmental exposures vary widely, making it difficult to isolate specific toxic effects. A more comprehensive map of the human lipidome in response to environmental toxins could lead to the development of biomarkers for early disease detection and improved understanding of exposure-related health risks. In the future, lipidomics may play a key role in personalizing health strategies by identifying lipid signatures linked to environmental pollutants, ultimately improving public health and disease prevention[118]. Remarkably, lipidomics is also being extended into space biology: combined microbiome and metabolomics analyses from the International Space Station have revealed environment-specific lipid and metabolite signatures, establishing a molecular framework for monitoring health during long-duration space missions[119].

Food and nutritional lipidomics: deciphering the complex role of lipids in diet and health

Lipidomics has become a widely adopted technology for studying the composition, nutritional value and health benefits of dietary lipids[120] (Fig. 2). Lipids play a crucial role in modulating metabolic health, and numerous studies have highlighted the potential of dietary interventions to regulate disease risk. For instance, the EPIC-Potsdam population-based cohort study utilized lipidomics to identify biomarkers for cardiovascular disease (CVD) and type 2 diabetes (T2D) risk, as well as to assess how these biomarkers respond to dietary interventions based on the content of saturated (SFA) and polyunsaturated fatty acids (PUFA)[121]. Dietary lipids can also influence the composition and metabolic activity of the gut microbiome. A Western-style, high-fat diet rich in SFA has been shown to induce shifts in gut microbial communities[122]. Importantly, it is not only the fatty acyl composition of foods that affects health, but also the structural features and complex interactions between lipids and other nutrients. As research on the role of lipids in human diets grows, there is increasing recognition of the need to understand food compositions beyond the traditional focus on total fat, fatty acid composition, and cholesterol[123]. This highlights the importance of more precise food profiling using advanced lipidomics technologies[124]. Additionally, food lipidomes vary depending on factors such as food type, genetic background, geographical origin, and climate. For example, lipidomic analysis of 155 agricultural products from 58 species across 23 plant families revealed differences not only at the level of species origin but also in the specific plant tissues, such as leaf, stem, seed, and caryopsis[125]. Consequently, lipidomics has emerged as a powerful tool for assessing food quality but also authenticity and traceability[126]. Furthermore, food processing and storage can alter the lipid composition by promoting lipid degradation and oxidation[127]. Lipidomics allows the quantification of lipid peroxidation products and the evaluation of food matrix stability across different processing stages, thus aiding in the optimization of industrial production processes[128,129].

Recent advancements in MS technologies provide significant benefits. For instance, rapid evaporation-ionization MS (REIMS) enables the direct analysis of both raw and processed food products, offering a reliable point-control method[130]. Additionally, the growth and broader use of structural lipidomics will enhance our understanding of lipid isomeric structures and their role in influencing sensory quality, stability, bioavailability, and the health effects of food products[131,132]. Lipidomics breakthroughs have also led to the discovery of bioactive compounds in food, such as plant-derived oxylipins, which can regulate inflammation and immune responses in consumers[133], and TG-estolides, which serve as precursors to a novel class of fatty acid esters, FAHFAs, with antidiabetic potential[134]. Moving forward, a concerted effort to standardize and harmonize food lipidomics, through both analytical techniques and data integration strategies, is essential. Integrating lipid profile data across various food matrices into specialized databases (e.g., FoodDB and FoodData Central[135]) would greatly support comprehensive, omics-based food research[136]. Mapping chemical exposures from diet will provide valuable insights to enhance health and reduce disease risk. Moreover, combining lipidomics data on dietary responses with GWAS focused on health outcomes will facilitate the development of nutrigenetic strategies, leading to personalized dietary recommendations[137,138].

The current deficit of dietary lipids to be produced and consumed according to WHO recommendations is estimated as 45 megaton (Mt) per year, which is projected to grow to 113 Mt by 2050[139]. However, compared to proteins, the composition and nutritional quality of lipids have received less focus when assessing food system sustainability. Lipidomics offers a powerful tool for developing sustainable strategies for lipid production, including the exploration of alternative food sources such as microalgae, new crops, insects, and even microbes[140,141]. For food producers and stakeholders, understanding how environmental factors, agricultural practices, processing, and preservation influence lipid quality is crucial to ensuring food safety, nutrition, and overall quality.

Exploring lipidomes across the tree of life: mapping the molecular basis of diversity and evolution

Recent discoveries underscore the minimal lipid requirements for life, with evidence that as few as two lipid species can sustain a minimal cell[142]. In striking contrast, lipid structural diversity across the Tree of Life is extensive. Despite conserved cellular architecture and core membrane functions, lipid composition varies widely among taxa, reflecting genetic, morphological and physiological adaptations to diverse ecological niches. Understanding the evolutionary and

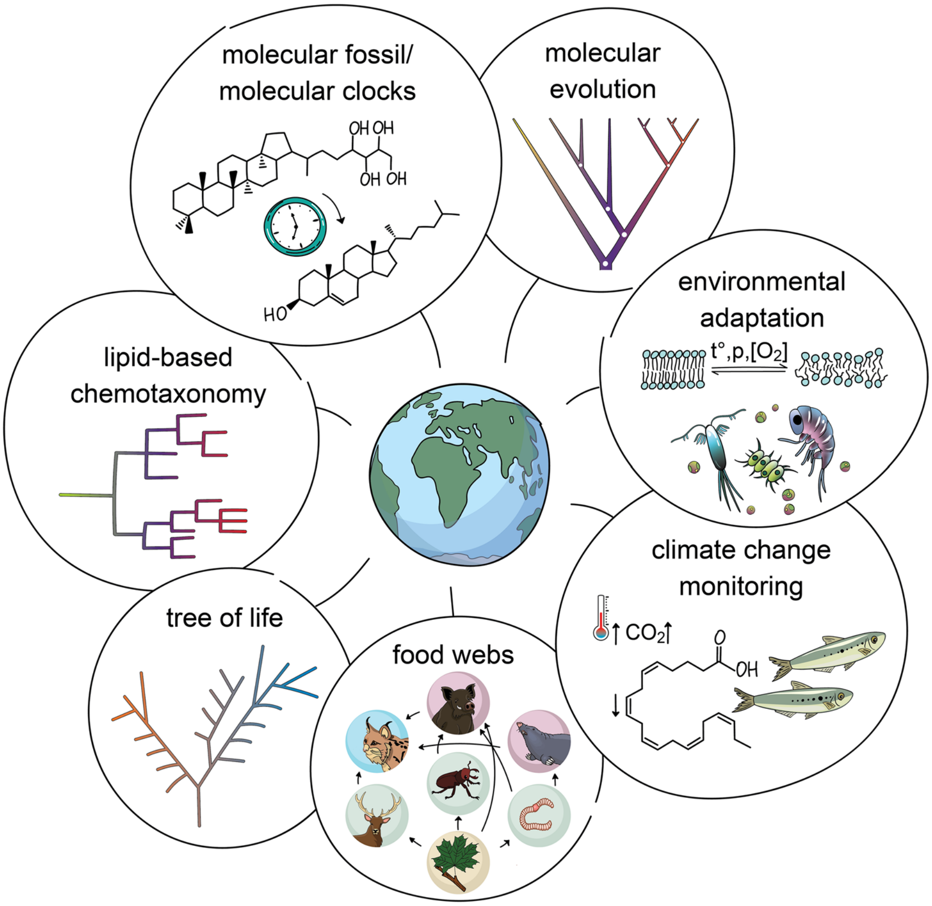

Fig. 3 | Lipidomics in Earth and environmental sciences. The expanding role of lipidomics in uncovering lipid biodiversity and tracing the evolution of lipidomes and metabolic pathways across the kingdoms of life. The figure highlights the ecological relevance of lipids in structuring food webs and regulating ecosystem dynamics, their role in organismal adaptation to environmental conditions, and the potential of lipidomic profiles as indicators for monitoring ecosystem health and assessing the impact of climate change.

functional basis of this diversification requires comprehensive qualitative and quantitative lipidome profiling across biological diversity (Fig. 3).

Recent advances in structural lipidomics, combined with phylogenetic approaches, are providing new insight into molecular evolution and species divergence. A key concept is the "lipid divide", the deep biochemical separation between archaeal membranes, composed of isoprenoid ether-linked glycerol-1-phosphate (G1P) forming monolayers, and bacterial/eukaryotic membranes, composed of fatty acid ester-linked glycerol-3-phosphate (G3P) bilayers. This dichotomy is thought to have emerged after the Last Universal Common Ancestor (LUCA), leaving its membrane composition unresolved. One hypothesis proposes that LUCA had a mixed, heterochiral membrane containing both lipid types, which, due to its chemical instability, diverged into archaeal and bacterial architectures, giving rise to the "lipid divide". This long-standing model has recently regained attention. An engineered *E. coli* strain producing both archaeal and bacterial phospholipids was shown to form stable hybrid membranes, challenging the assumption that mixed systems are inherently unstable[143]. In contrast, studies in *Mycoplasma mycoides* suggest that mixed lipid populations can impair membrane function, but likely through disrupted lipid-protein interactions rather than altered bilayer physics[142]. Recent discoveries of microorganisms with naturally occurring mixed membranes add a new dimension to this debate. Combined lipidomic and comparative genomic analyses indicate that members of the bacterial *Fibrobacteres-Chlorobi-Bacteroidetes* superphylum harbour a complete archaeal-like lipid-synthesis pathway[144], whereas certain members of the archaeal Asgard superphylum encode components of the bacterial lipid-biosynthetic route[145]. The co-occurrence of both biosynthetic machineries may indeed support the existence of a mixed-membrane state in LUCA, offering a plausible bridge across the "lipid divide".

Systematic efforts to map lipid diversity across phylogenetic lineages are still in their early stages. While many lipid classes are evolutionarily conserved, the abundance and composition of their molecular species often vary markedly between taxa[146]. In addition, some lipid subclasses appear to be clade-specific: for example, glycoglycerolipids are typical of photosynthetic organisms, including algae and plants, while betaine lipids are found in algae, bryophytes, and some fungi, but are absent in seed plants[147]. Structural lipidomics continues to uncover novel lipid subclasses, such as maradolipids[12] and phosphorylated glycosphingolipids[148] in nematodes or phosphatidylhomoserine species in *E. coli*[149], suggesting that a substantial fraction of lipid diversity remains unexplored. For newly identified lipids, functional assignment can be challenging. However, because structurally related lipids often share functional roles, comparative lipidomics provides a powerful framework for inferring lipid class biology. Maradolipids, glycolipids with a trehalose headgroup first identified in bacteria such as *Mycobacterium* and *Corynebacterium* and later found in *C. elegans*[12], illustrate this principle. Although their functions remain incompletely defined, their enrichment in bacterial cell walls suggests roles in membrane permeability and barrier properties that are likely conserved in nematodes. Furthermore, for model

BOX 5

The comparative lipidomics approach reveals conserved biochemical motifs and traces the evolutionary lipid distribution

Lipids are more resistant to diagenetic degradation than proteins or nucleic acids, thus structural lipid features can persist in the geological record. Sterol lipids provide key examples. Saturated steranes and hopanes, derived from sterols and hopanoids, are widely used in sedimentary rocks as proxies for eukaryotic and bacterial biomass in ancient ecosystems[187]. Distinct sterol side-chain structures enable taxonomic inference: C27 sterols (e.g., cholesterol) are characteristic of eumetazoans and red algae, C28 sterols of fungi, and C29 sterols of plants and green algae. Comparative lipidomics of fossil steranes, combined with genomics, can identify organisms capable of producing specific sterol classes and constrain when these pathways evolved[188,189]. Thus, sterols and hopanoids act as molecular fossils preserved in sediments and are increasingly used as biomarkers and molecular clocks to track the co-evolution of metabolic pathways and lineages[187].

organisms such as *C. elegans*, *D. melanogaster*, and mice the integration of genetic tools with lipidomic profiling, supports detailed studies of lipid function and regulation[150,151]. Emerging multi-omics approaches that combine lipidomics with transcriptomic and proteomic data, alongside refined comparative algorithms such as the LUX score[152,153], are poised to generate mechanistic insights into lipid function and evolution across broad taxonomic groups (Box 5).

Uncovering novel lipid subclasses, particularly in underexplored clades, requires combining high-resolution structural lipidomics with validation approaches such as labelling and metabolic incorporation[149]. Often next-generation de novo annotation strategies that go beyond conventional spectral library matching are required. The structural complexity of uncharacterized lipids often necessitates manual interpretation or the development of specialized computational pipelines[154]. To accelerate discovery, new algorithms are being developed, including molecular networking and reverse lipidomics, which allow annotation based on shared structural motifs rather than exact spectral matches. These efforts are increasingly supported by large-scale data repositories and taxonomically informed tools such as microbeMASST and plantMASST, which link LC-MS/MS spectra to over 1,300 microbial and 2,800 plant species, respectively[155,156]. Platforms like GNPS (Global Natural Products Social Molecular Networking)[78] further enable molecular networking to reveal structural relationships among unknown lipids. Together, these integrative advances are transforming lipidomics into a powerful chemotaxonomic tool, capable of revealing both deep evolutionary relationships and environmentally driven adaptations across the Tree of Life.

Lipidomics in eco-evo-devo research: uncovering the molecular dynamics of ecosystem evolution

Lipids are increasingly appreciated as critical molecular markers for probing structure, connectivity, and function of ecosystems across the biosphere (Fig. 3). Lipidomics has emerged as a powerful approach to explore the ecological, evolutionary, and developmental (eco-evo-devo) roles of essential dietary lipids, offering fresh insights into the molecular foundations of biodiversity and ecosystem dynamics. Fatty acid (FA) profiling is widely used in both aquatic and terrestrial environments to trace trophic pathways and delineate food web architecture. The heterogeneous spatiotemporal distribution of dietary lipids mirrors complex biotic interactions and abiotic factors[157]. Despite their ubiquity, FAs display notable qualitative or quantitative specificity and diversity across taxa: bacterial branched-chain and cyclopropane FAs, ω−3 PUFAs from microalgae, enrichment of oleic acid in plants or linoleic acid in fungi serve as distinctive trophic biomarkers. This specificity makes FA profiling a valuable tool for ecological network analysis because of the “dietary routing” (i.e., incorporation of the food FA biomarkers into consumer’s lipidome). Advanced statistical frameworks such as Quantitative Fatty Acid Signature Analysis (QFASA) and Bayesian source-tracing models have been developed to reconstruct consumer diets from FA data in marine and terrestrial systems[158–161]. More broadly, the emerging field of ecological lipidology situates lipidomics as a lens to address fundamental questions in biodiversity, adaptation, and macroevolution, including the fitness consequences of lipid-specific foraging and the evolutionary impact of sterol or PUFA auxotrophy[162].

Lipidomics has advanced our understanding of environmental adaptation by revealing how membrane lipid composition responds to changing conditions. For instance, the ratio of saturated to unsaturated acyl chains in membrane lipids provides a sensitive indicator of homeoviscous adaptation in poikilothermic organisms such as bacteria, algae, and plants, enabling the maintenance of membrane fluidity across temperature gradients[163]. Recent studies of deep-sea fauna have implicated plasmalogens as critical to homeocurvature adaptation, supporting membrane integrity under extreme hydrostatic pressure[164]. While lipids have long served as biomarkers in oceanographic research[117], their application at the lipidomics scale is more recent. A global survey of marine plankton lipidomes across 146 sites uncovered a strong correlation between lipid unsaturation indices and ocean temperature[165]. Crucially, temperature-induced variations in eicosapentaenoic acid levels enabled projections of its availability under future climate scenarios, highlighting potential risks to the nutritional quality of marine food webs.

Despite significant advances, wide application of lipidomics in ecosystem research faces several challenges. The vast functional diversity of lipidomes across species, especially those adapted to extreme or specialized niches, remains largely uncharted, with many lipid species still unidentified. Accessing such organisms often necessitates costly, logistically complex expeditions[166]. Although lipidomics in eco-evo-devo research is nascent, expanding lipidome coverage beyond traditional model organisms has already demonstrated substantial promise. Comprehensive profiling of FA concentrations and distributions across diverse taxa is essential to discern the specificity and universality of lipid-based biomarkers, which could be expressed in either absolute or relative terms. To date, marine food webs have received more extensive lipidomic characterization than terrestrial systems. To address this disparity, a lipid library covering 50 basal resource species in soil food webs, including algae, bacteria, fungi, and plants, has recently been developed to enhance FA signature resolution and resource classification in terrestrial ecosystems[167]. However, integration of FA profiles across ecosystem boundaries, linking aquatic, terrestrial, above- and below-ground networks, remains limited, hindering efforts to resolve primary FA sources and trophic pathways at ecosystem and biosphere scales. Understanding how climate change, land use, and other environmental pressures reshape FA trafficking and distribution is vital for predicting ecosystem resilience, supporting bioremediation, guiding conservation, and safeguarding biodiversity and human nutrition.

BOX 6

Open questions and future directions in lipidomics

- Implementation of rigorous quality assurance frameworks and standardized operating procedures (for example, community-driven Lipidomics Minimal Reporting Checklist) to overcome current limitations in robustness and reproducibility
- Elucidation of the full complexity of natural lipidomes, including discovery of new lipid subclasses and deeper structural annotation of known species, particularly double-bond positional isomers.
- Resolution of cell-type and context specific lipid heterogeneity within tissues through high-resolution spatial lipidomics.
- Moving beyond static measurements towards dynamic analyses that capture lipidome plasticity and metabolic flux.
- Advancing from compositional cataloguing to functional lipidomics, addressing collective lipid behaviour and its mechanistic roles in biological systems.
- Improving interoperability among lipidomics datasets generated using diverse software platforms, partially addressed by emerging lipid annotation conversion tools and harmonized shorthand notation.
- Systematic characterization of novel lipid species through reverse lipidomics strategies and molecular networking frameworks.
- Development of robust computational approaches for multi-omics data integration.
- A conceptual shift towards functional lipidomics, requiring integrative frameworks that combine biochemical and biological knowledge with lipidomics-derived datasets.

Future perspectives in lipidomics

A remarkable expansion in lipidomics technologies, supported by the parallel development of computational tools, has positioned lipidomics and its applications at the forefront of modern biology and biomedicine. However, several open questions remain and define future directions in technological development (Box 6). Among these, a key challenge is the functional interpretation of lipid compositional changes. Current views on lipid functions are largely centred around biochemical pathways[168,169], biophysical ontologies[170], and fragmented knowledge of lipid-protein interactions in signalling. However, lipids rarely act at the level of individual species; instead, they function as supramolecular assemblies in the form of organelle-specific membranes and specialized membrane domains. Such lipid collectives most likely represent the true functional units responsible for biological activity; however, they remain challenging to define both qualitatively and quantitatively[171]. As knowledge in lipid biochemistry continues to expand, bridging the gap between lipidomics and function will require close collaboration between classical lipid biologists and analytical experts. Recent efforts to generate lipid atlases at increasing levels of spatial resolution (including subcellular structures[172], specific cell types[36]) and distinct tissues and organs[41,173], represent important steps toward contextualizing lipid function. Leveraging the expanding knowledge base, tools such as LIPID MAPS Reaction Explorer can support the association of lipid species with corresponding proteins and genes, thereby facilitating cross-omics data integration. Moreover, the growing accessibility of omics technologies is enabling the simultaneous generation of multi-omics data from the same experimental systems, and new computational frameworks are being developed to support integrative, data- and knowledge-driven analyses[174–176]. This will be a critical step toward achieving functional lipidomics.

Given the centrality of lipids to physiology across scales, the integration of lipidomics into biomedical research has strong potential for diagnostics and clinical translation. Major hurdles here will be the clinical performance validation, regulatory challenges, acceptance and finally implementation of such assays in a clinical setting, preferably with metrologically traceable, molar concentrations. Lipidomics enables the discovery of biomarkers across a broad spectrum of human diseases with advances in structural lipidomics further illuminating metabolic plasticity in diverse cancers[177] and revealing previously unrecognized lipid diversity in bacteria[149]. These insights are informing the development of personalized therapies and uncovering novel mechanisms that may be exploited to combat antimicrobial resistance. Lipidomics also becomes powerful tool for understanding the biology of ageing. Lipid alterations have emerged as robust correlates of biological age[4], culminating in the development of “Lipid Ageing Clocks”[178]. Notably, lipidomic studies have revealed pronounced sexual dimorphism in lipidome remodelling during healthy ageing and disease development, exposing persistent gaps in biomedical knowledge and therapeutic designs. These findings directly support gender equality by underscoring the need for sex-inclusive biomedical research.

Although the majority of lipidomics research has focused on human biology, its applications increasingly extend to environmental monitoring. Lipid biomarkers are emerging as sensitive indicators of ecosystem health[117]. The integration of lipidomic data in ecological monitoring and food web analysis positions lipidomics at the forefront of efforts to track and predict environmental change, making it an essential tool for exploring dynamic biosphere processes on a planetary scale. Advances in food lipidomics are becoming instrumental in shaping sustainable food systems and responsible production practices. These efforts illuminate the deep interdependence between ecosystem integrity and human health. In the broader context of human health and global food security, modern food and biotechnology industries are increasingly recognizing the value of data generated by lipidomics for assessing nutritional value, product safety, and quality control, and advancing personalized nutrition strategies. Lipidomics research now transcends human health and stretches to global benefit: it is being applied to study the molecular organization of organisms across all domains of life, offering insights into evolutionary biology and ecosystem function.

Conclusion

The remarkable growth that lipidomics has experienced over the last two decades has been driven by advances in MS-based instrumentation and the parallel evolution of sophisticated bioinformatics tools capable of handling high-throughput data processing. The maturation of lipidomics has been propelled by coordinated efforts focused on education, collaboration, and standardization (Box 7). As lipidomics has evolved into a mature and versatile analytical discipline, it is increasingly well positioned to contribute to solutions addressing a range of societal challenges. Looking forward, continued technological innovation and interdisciplinary collaboration will be crucial to unlocking the full potential of lipidomics: from personalized medicine to sustainable ecosystem management, and heralding a new era of lipid-centred discoveries and applications.

BOX 7

Community-driven and collaborative efforts in lipidomics

Since its establishment in 2003, LIPID MAPS has served as a cornerstone resource, providing curated lipid databases, analytical tools, and educational materials that continue to guide the global lipidomics community. The Pan-European Network in Lipidomics and Epilipidomics (EpiLipidNET), launched in 2021 under the EU COST programme, now connects over 450 researchers across multiple disciplines, fostering collaborative research and knowledge exchange. On a global scale, the International Lipidomics Society (ILS), founded in 2019, champions open communication, data transparency, and methodological harmonization. The LipidMet Interest Group within the Metabolomics Society further bridges lipidomics and metabolomics fields, advancing integrated systems for metabolism research. These initiatives have been instrumental in developing best practices and quality assurance frameworks. For example, the Lipidomics Minimal Reporting Checklist, introduced by ILS and the Lipid Standards Initiative (LSI)[52], standardizes the evaluation of lipidomics data quality in publications. The Oxylipin Analysis Interest Group has published detailed guidelines addressing technical and interpretative challenges specific to oxylipin workflows[190]. Meanwhile, LIPID MAPS continues to expand by integrating community-generated oxylipin spectral libraries and, together with EpiLipidNET, hosts the Lipidomics Tools Guide to aid bioinformatics tool selection[53]. Importantly, ILS-led ring trials targeting quantitative analysis of clinically relevant lipids such as ceramides and bile acids in standard matrices like human plasma, mark crucial milestones toward clinical implementation. As these international networks grow, they not only strengthen scientific collaboration but also lay the foundation for applying lipidomics to address urgent societal challenges, ranging from public health and precision medicine to food security and environmental sustainability, thus solidifying lipidomics as a versatile platform with broad scientific and translational impact.

References

1. Harayama, T. & Riezman, H. Understanding the diversity of membrane lipid composition. *Nat. Rev. Mol. Cell Biol.* **19**, 281–296 (2018).
2. Sezgin, E., Levental, I., Mayor, S. & Eggeling, C. The mystery of membrane organization: composition, regulation and roles of lipid rafts. *Nat. Rev. Mol. Cell Biol.* **18**, 361–374 (2017).
3. Schneider, K. M. et al. The Lipidomic Profile Discriminates Between MASLD and MetALD. *Aliment. Pharmacol. Ther.* **61**, 1357–1371 (2025).
4. Hornburg, D. et al. Dynamic lipidome alterations associated with human health, disease and ageing. *Nat. Metab.* **5**, 1578–1594 (2023).
5. Stegemann, C. et al. Lipidomics profiling and risk of cardiovascular disease in the prospective population-based Bruneck study. *Circulation* **129**, 1821–1831 (2014).
6. Gross, R. W. The evolution of lipidomics through space and time. *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **1862**, 731–739 (2017).
7. Han, X. & Gross, R. W. The foundations and development of lipidomics. *J. Lipid Res.* **63**, 100164 (2022).
8. Covey, T. R. Forty-Year Evolution of High-Throughput Mass Spectrometry. in *High-Throughput Mass Spectrometry in Drug Discovery* 1–74 (Wiley, 2023). https://doi.org/10.1002/9781119678496.ch1.
9. Covey, T. Where have all the ions gone, long time passing? Tandem quadrupole mass spectrometers with atmospheric pressure ionization sensitivity gains since the mid-1970s. A perspective. *Rapid Commun. Mass Spectrom.* **39**, e9354 (2025).
10. Peterka, O. et al. HILIC/MS quantitation of low-abundant phospholipids and sphingolipids in human plasma and serum: dysregulation in pancreatic cancer. *Anal. Chim. Acta* **1288**, 342144 (2024).
11. Huynh, K. et al. High-throughput plasma lipidomics: detailed mapping of the associations with cardiometabolic risk factors. *Cell Chem. Biol.* **26**, 71–84.e4 (2019).
12. Penkov, S. et al. Maradolipids: diacyltrehalose glycolipids specific to dauer larva in Caenorhabditis elegans. *Angew. Chem. Int. Ed. Engl.* **49**, 9430–9435 (2010).
13. Lavrynenko, O. et al. The ecdysteroidome of Drosophila: influence of diet and development. *Development* **142**, 3758–3768 (2015).
14. Bilgin, M. et al. Lipid discovery by combinatorial screening and untargeted LC-MS/MS. *Sci. Rep.* **6**, 27920 (2016).
15. Leaptrot, K. L., May, J. C., Dodds, J. N. & McLean, J. A. Ion mobility conformational lipid atlas for high confidence lipidomics. *Nat. Commun.* **10**, 985 (2019).
16. Young, R. S. E. et al. Apocryphal FADS2 activity promotes fatty acid diversification in cancer. *Cell Rep.* **34**, 108738 (2021).
17. Xia, T. et al. Deep-profiling of phospholipidome via rapid orthogonal separations and isomer-resolved mass spectrometry. *Nat. Commun.* **14**, 4263 (2023).
18. Uchino, H., Tsugawa, H., Takahashi, H. & Arita, M. Computational mass spectrometry accelerates C = C position-resolved untargeted lipidomics using oxygen attachment dissociation. *Commun. Chem.* **5**, 162 (2022).
19. Method of the Year 2024: spatial proteomics. *Nat. Methods* **21**, 2195–2196 (2024).
20. Calvo, I. et al. Lipid imaging mass spectrometry: towards a new molecular histology. *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **1870**, 159568 (2025).
21. Soltwisch, J. et al. MALDI-2 on a trapped ion mobility quadrupole time-of-flight instrument for rapid mass spectrometry imaging and ion mobility separation of complex lipid profiles. *Anal. Chem.* **92**, 8697–8703 (2020).
22. Kompauer, M., Heiles, S. & Spengler, B. Atmospheric pressure MALDI mass spectrometry imaging of tissues and cells at 1.4-μm lateral resolution. *Nat. Methods* **14**, 90–96 (2017).
23. Amer, S., Unsihuay, D., Yang, M. & Laskin, J. Universal photosensitizer for isomer-selective lipid imaging with high molecular coverage. *Anal. Chem.* **97**, 7071–7078 (2025).
24. Farrow, M. A. et al. A lipid atlas of the human kidney. *Sci. Adv.* **11**, eadu3730 (2025).
25. Xie, Y. R. et al. Multiscale biochemical mapping of the brain through deep-learning-enhanced high-throughput mass spectrometry. *Nat. Methods* **21**, 521–530 (2024).
26. Vandenbosch, M. et al. Toward omics-scale quantitative mass spectrometry imaging of lipids in brain tissue using a multiclass internal standard mixture. *Anal. Chem.* **95**, 18719–18730 (2023).
27. Goossens, P. et al. Integrating multiplex immunofluorescent and mass spectrometry imaging to map myeloid heterogeneity in its metabolic and cellular context. *Cell Metab.* **34**, 1214–1225.e6 (2022).
28. Bonhommeau, S., Cooney, G. S. & Huang, Y. Nanoscale chemical characterization of biomolecules using tip-enhanced Raman spectroscopy. *Chem. Soc. Rev.* **51**, 2416–2430 (2022).

29. Hendriks, T. F. E. et al. MALDI-MSI-LC-MS/MS Workflow for single-section single step combined proteomics and quantitative lipidomics. *Anal. Chem.* **96**, 4266–4274 (2024).
30. Nunes, J. B. et al. Integration of mass cytometry and mass spectrometry imaging for spatially resolved single-cell metabolic profiling. *Nat. Methods* **21**, 1796–1800 (2024).
31. Chen, P.-H. B., Li, X.-L. & Baskin, J. M. Synthetic lipid biology. *Chem. Rev.* **125**, 2502–2560 (2025).
32. Wunderling, K., Zurkovic, J., Zink, F., Kuerschner, L. & Thiele, C. Triglyceride cycling enables modification of stored fatty acids. *Nat. Metab.* **5**, 699–709 (2023).
33. Thiele, C., Wunderling, K. & Leyendecker, P. Multiplexed and single cell tracing of lipid metabolism. *Nat. Methods* **16**, 1123–1130 (2019).
34. Nepachalovich, P. et al. LC-MS and high-throughput data processing solutions for lipid metabolic tracing using bioorthogonal click chemistry. *Angew. Chem. Int. Ed. Engl.* **64**, e202501884 (2025).
35. Salvador, A. F., Shyu, C.-R. & Parks, E. J. Measurement of lipid flux to advance translational research: evolution of classic methods to the future of precision health. *Exp. Mol. Med.* **54**, 1348–1353 (2022).
36. Morgan, P. K. et al. A lipid atlas of human and mouse immune cells provides insights into ferroptosis susceptibility. *Nat. Cell Biol.* **26**, 645–659 (2024).
37. Osetrova, M. et al. Lipidome atlas of the adult human brain. *Nat. Commun.* **15**, 4455 (2024).
38. Tsugawa, H. et al. A lipidome landscape of aging in mice. *Nat. Aging* **4**, 709–726 (2024).
39. Ding, J. et al. A metabolome atlas of the aging mouse brain. *Nat. Commun.* **12**, 6021 (2021).
40. Folz, J. et al. Human metabolome variation along the upper intestinal tract. *Nat. Metab.* **5**, 777–788 (2023).
41. Lange, M. et al. AdipoAtlas: a reference lipidome for human white adipose tissue. *Cell Rep. Med.* **2**, 100407 (2021).
42. Köfeler, H. C. et al. Quality control requirements for the correct annotation of lipidomics data. *Nat. Commun.* **12**, 4771 (2021).
43. Cochran, D. et al. A reproducibility crisis for clinical metabolomics studies. *Trends Analyt. Chem.* **180**, 117918 (2024).
44. Lipidomics Standards Initiative Consortium Lipidomics needs more standardization. *Nat. Metab.* **1**, 745–747 (2019).
45. Koelmel, J. P., Ulmer, C. Z., Jones, C. M., Yost, R. A. & Bowden, J. A. Common cases of improper lipid annotation using high-resolution tandem mass spectrometry data and corresponding limitations in biological interpretation. *Biochim. Biophys. Acta Mol. Cell Biol. Lipids* **1862**, 766–770 (2017).
46. Wölk, M. & Fedorova, M. Recommendations for accurate lipid annotation and semi-absolute quantification from LC-MS/MS datasets. *Methods Mol. Biol.* **2855**, 269–287 (2025).
47. Bishop, L. M., Shen, T. & Fiehn, O. Improving quantitative accuracy in nontargeted lipidomics by evaluating adduct formation. *Anal. Chem.* **95**, 12683–12690 (2023).
48. Metz, T. O. et al. Introducing 'Identification Probability' for automated and transferable assessment of metabolite identification confidence in metabolomics and related studies. *Anal. Chem.* **97**, 1–11 (2025).
49. Witting, M. et al. Challenges and perspectives for naming lipids in the context of lipidomics. *Metabolomics* **20**, 15 (2024).
50. Liebisch, G. et al. Update on LIPID MAPS classification, nomenclature, and shorthand notation for MS-derived lipid structures. *J. Lipid Res.* **61**, 1539–1555 (2020).
51. McDonald, J. G. et al. Introducing the lipidomics minimal reporting checklist. *Nat. Metab.* **4**, 1086–1088 (2022).
52. Kopczynski, D. et al. The lipidomics reporting checklist a framework for transparency of lipidomic experiments and repurposing resource data. *J. Lipid Res.* **65**, 100621 (2024).
53. Ni, Z. et al. Guiding the choice of informatics software and tools for lipidomics research applications. *Nat. Methods* **20**, 193–204 (2023).
54. Takeda, H. et al. MS-DIAL 5 multimodal mass spectrometry data mining unveils lipidome complexities. *Nat. Commun.* **15**, 9903 (2024).
55. Schmid, R. et al. Integrative analysis of multimodal mass spectrometry data in MZmine 3. *Nat. Biotechnol.* **41**, 447–449 (2023).
56. Witting, M., Ruttkies, C., Neumann, S. & Schmitt-Kopplin, P. LipidFrag: Improving reliability of in silico fragmentation of lipids and application to the Caenorhabditis elegans lipidome. *PLoS One* **12**, e0172311 (2017).
57. Dührkop, K. et al. SIRIUS 4: a rapid tool for turning tandem mass spectra into metabolite structure information. *Nat. Methods* **16**, 299–302 (2019).
58. Takeda, H. et al. Dual fragmentation via collision-induced and oxygen attachment dissociations using water and its radicals for C=C position-resolved lipidomics. *Commun. Chem.* **8**, 148 (2025).
59. Tortorella, S. et al. LipostarMSI: comprehensive, vendor-neutral software for visualization, data analysis, and automated molecular identification in mass spectrometry imaging. *J. Am. Soc. Mass Spectrom.* **31**, 155–163 (2020).
60. Zhang, W. et al. Integration of Multiple Spatial Omics Modalities Reveals Unique Insights into Molecular Heterogeneity of Prostate Cancer. Preprint at https://doi.org/10.1101/2023.08.28.555056 (2023).
61. Dehairs, J. et al. LipidQMap - An Open-Source Tool for Quantitative Mass Spectrometry Imaging of Lipids. Preprint at https://doi.org/10.1101/2025.10.15.682422 (2025).
62. Hu, H. & Laskin, J. Emerging computational methods in mass spectrometry imaging. *Adv. Sci. (Weinh.).* **9**, e2203339 (2022).
63. Ellis, S. R. et al. Automated, parallel mass spectrometry imaging and structural identification of lipids. *Nat. Methods* **15**, 515–518 (2018).
64. Kambhampati, S. et al. SIMPEL: using stable isotopes to elucidate dynamics of context specific metabolism. *Commun. Biol.* **7**, 172 (2024).
65. Ni, Z. & Fedorova, M. LipidLynxX: a data transfer hub to support integration of large scale lipidomics datasets. Preprint at https://doi.org/10.1101/2020.04.09.033894 (2020).
66. Kopczynski, D., Hoffmann, N., Peng, B. & Ahrends, R. Goslin: a grammar of succinct lipid nomenclature. *Anal. Chem.* **92**, 10957–10960 (2020).
67. Conroy, M. J. et al. LIPID MAPS: update to databases and tools for the lipidomics community. *Nucleic Acids Res.* **52**, D1677–D1682 (2024).
68. Aimo, L. et al. The SwissLipids knowledgebase for lipid biology. *Bioinformatics* **31**, 2860–2866 (2015).
69. Watanabe, K., Yasugi, E. & Oshima, M. How to Search the Glycolipid data in 'LIPIDBANK for Web' the Newly Developed Lipid Database in Japan. *Trends Glycosci. Glycotechnol.* **12**, 175–184 (2000).
70. Sud, M. et al. Metabolomics Workbench: An international repository for metabolomics data and metadata, metabolite standards, protocols, tutorials and training, and analysis tools. *Nucleic Acids Res.* **44**, D463–D470 (2016).
71. Yurekten, O. et al. MetaboLights: open data repository for metabolomics. *Nucleic Acids Res.* **52**, D640–D646 (2024).
72. da Silva, R. R., Dorrestein, P. C. & Quinn, R. A. Illuminating the dark matter in metabolomics. *Proc. Natl. Acad. Sci. USA* **112**, 12549–12550 (2015).

73. Uritboonthai, W., Hoang, L., Aisporna, A., Giera, M. & Siuzdak, G. The dark metabolome/lipidome and in-source fragmentation. *Anal. Sci. Adv.* **6**, e70012 (2025).
74. Xu, H. et al. LipidIN: a comprehensive repository for flash platform-independent annotation and reverse lipidomics. *Nat. Commun.* **16**, 4566 (2025).
75. Elloumi, A. et al. From MS/MS library implementation to molecular networks: Exploring oxylipin diversity with NEO-MSMS. *Sci. Data* **11**, 193 (2024).
76. Gentry, E. C. et al. Reverse metabolomics for the discovery of chemical structures from humans. *Nature* **626**, 419–426 (2024).
77. Charron-Lamoureux, V. et al. A guide to reverse metabolomics-a framework for big data discovery strategy. *Nat. Protoc.* **20**, 2960–2993 (2025).
78. Aron, A. T. et al. Reproducible molecular networking of untargeted mass spectrometry data using GNPS. *Nat. Protoc.* **15**, 1954–1991 (2020).
79. Damiani, T. et al. A universal language for finding mass spectrometry data patterns. *Nat. Methods* **22**, 1247–1254 (2025).
80. Vvedenskaya, O. et al. Nonalcoholic fatty liver disease stratification by liver lipidomics. *J. Lipid Res.* **62**, 100104 (2021).
81. Huynh, K. et al. Concordant peripheral lipidome signatures in two large clinical studies of Alzheimer's disease. *Nat. Commun.* **11**, 5698 (2020).
82. Wolrab, D. et al. Lipidomic profiling of human serum enables detection of pancreatic cancer. *Nat. Commun.* **13**, 124 (2022).
83. Vvedenskaya, O. et al. Clinical lipidomics—a community-driven roadmap to translate research into clinical applications. *J. Mass Spectrom. Adv. Clin. lab* **24**, 1–4 (2022).
84. Kvasnička, A. et al. Clinical lipidomics in the era of the big data. *Clin. Chem. Lab. Med.* **61**, 587–598 (2023).
85. Julkunen, H. et al. Atlas of plasma NMR biomarkers for health and disease in 118,461 individuals from the UK Biobank. *Nat. Commun.* **14**, 604 (2023).
86. Wilcken, B., Wiley, V., Hammond, J. & Carpenter, K. Screening newborns for inborn errors of metabolism by tandem mass spectrometry. *N. Engl. J. Med.* **348**, 2304–2312 (2003).
87. Videbæk, C., Melgaard, L., Lund, A. M. & Grønborg, S. W. Newborn screening for adrenoleukodystrophy: International experiences and challenges. *Mol. Genet. Metab.* **140**, 107734 (2023).
88. Kemper, A. R. et al. Newborn screening for X-linked adrenoleukodystrophy: evidence summary and advisory committee recommendation. *Genet. Med.* **19**, 121–126 (2017).
89. Tang, C. et al. A pilot study of newborn screening for X-linked adrenoleukodystrophy based on liquid chromatography-tandem mass spectrometry method for detection of C26:0-lysophosphatidylcholine in dried blood spots: results from 43,653 newborns in a southern Chinese population. *Clin. Chim. Acta* **552**, 117653 (2024).
90. Graham, S. E. et al. The power of genetic diversity in genome-wide association studies of lipids. *Nature* **600**, 675–679 (2021).
91. Ottensmann, L. et al. Genome-wide association analysis of plasma lipidome identifies 495 genetic associations. *Nat. Commun.* **14**, 6934 (2023).
92. Cadby, G. et al. Comprehensive genetic analysis of the human lipidome identifies loci associated with lipid homeostasis with links to coronary artery disease. *Nat. Commun.* **13**, 3124 (2022).
93. Tarasov, K. et al. Molecular lipids identify cardiovascular risk and are efficiently lowered by simvastatin and PCSK9 deficiency. *J. Clin. Endocrinol. Metab.* **99**, E45–E52 (2014).
94. Laaksonen, R. et al. Plasma ceramides predict cardiovascular death in patients with stable coronary artery disease and acute coronary syndromes beyond LDL-cholesterol. *Eur. Heart J.* **37**, 1967–1976 (2016).
95. Meeusen, J. W. et al. Plasma ceramides. *Arterioscler. Thromb. Vasc. Biol.* **38**, 1933–1939 (2018).
96. Hilvo, M. et al. Development and validation of a ceramide- and phospholipid-based cardiovascular risk estimation score for coronary artery disease patients. *Eur. Heart J.* **41**, 371–380 (2020).
97. Wu, J. et al. Lipidomic risk score to enhance cardiovascular risk stratification for primary prevention. *J. Am. Coll. Cardiol.* **84**, 434–446 (2024).
98. Beyene, H. B. et al. Development and validation of a plasmalogen score as an independent modifiable marker of metabolic health: population based observational studies and a placebo-controlled cross-over study. *EBioMedicine* **105**, 105187 (2024).
99. Sales, S. et al. Gender, contraceptives and individual metabolic predisposition shape a healthy plasma lipidome. *Sci. Rep.* **6**, 27710 (2016).
100. Tabassum, R. et al. Lipidome- and genome-wide study to understand sex differences in circulatory lipids. *J. Am. Heart Assoc.* **11**, e027103 (2022).
101. Prabutzki, P. et al. Sex-specific lipidomic signatures in aortic valve disease reflect differential fibro-calcific progression. *Nat. Commun.* **16**, 5163 (2025).
102. Yang, K. & Han, X. Accurate quantification of lipid species by electrospray ionization mass spectrometry - Meet a key challenge in lipidomics. *Metabolites* **1**, 21–40 (2011).
103. Wang, M., Wang, C. & Han, X. Selection of internal standards for accurate quantification of complex lipid species in biological extracts by electrospray ionization mass spectrometry-What, how and why? *Mass Spectrom. Rev.* **36**, 693–714 (2017).
104. Bowden, J. A. et al. Harmonizing lipidomics: NIST interlaboratory comparison exercise for lipidomics using SRM 1950-Metabolites in Frozen Human Plasma. *J. Lipid Res.* **58**, 2275–2288 (2017).
105. Triebl, A. et al. Shared reference materials harmonize lipidomics across MS-based detection platforms and laboratories. *J. Lipid Res.* **61**, 105–115 (2020).
106. Torta, F. et al. Concordant inter-laboratory derived concentrations of ceramides in human plasma reference materials via authentic standards. *Nat. Commun.* **15**, 8562 (2024).
107. You, J. et al. Plasma proteomic profiles predict individual future health risk. *Nat. Commun.* **14**, 7817 (2023).
108. Nightingale Health Biobank Collaborative Group Metabolomic and genomic prediction of common diseases in 700,217 participants in three national biobanks. *Nat. Commun.* **15**, 10092 (2024).
109. Lai, Y., Ay, M., Hospital, C. D., Miller, G. W. & Sarkar, S. Seminar: functional exposomics and mechanisms of toxicity-insights from model systems and NAMs. *Environ. Health Perspect.* **132**, 94201 (2024).
110. Narzt, M.-S. et al. A novel role for NUPR1 in the keratinocyte stress response to UV oxidized phospholipids. *Redox Biol.* **20**, 467–482 (2019).
111. Narzt, M.-S. et al. Epilipidomics of senescent dermal fibroblasts identify lysophosphatidylcholines as pleiotropic senescence-associated secretory phenotype (SASP) factors. *J. Invest. Dermatol.* **141**, 993–1006.e15 (2021).
112. Ogrodnik, M. et al. Guidelines for minimal information on cellular senescence experimentation in vivo. *Cell* **187**, 4150–4175 (2024).
113. McGlinchey, A. et al. Prenatal exposure to perfluoroalkyl substances modulates neonatal serum phospholipids, increasing risk of type 1 diabetes. *Environ. Int.* **143**, 105935 (2020).
114. Hyötyläinen, T. et al. Lipidomic analyses reveal modulation of lipid metabolism by the PFAS perfluoroundecanoic acid (PFUnDA) in non-obese diabetic mice. *Front. Genet.* **12**, 721507 (2021).
115. Molina-Millán, L. et al. Mass spectrometry imaging enables detection of MPs and their effects in Daphnia magna following acute exposure. *Aquat. Toxicol.* **280**, 107253 (2025).

116. Liu, M. et al. Polypropylene microplastics triggered mouse kidney lipidome reprogramming combined with ROS stress as revealed by lipidomics and Raman biospectra. *Chemosphere* **370**, 143926 (2025).
117. Koelmel, J. P. et al. Environmental lipidomics: understanding the response of organisms and ecosystems to a changing world. *Metabolomics* **16**, 56 (2020).
118. Orešič, M., McGlinchey, A., Wheelock, C. E. & Hyötyläinen, T. Metabolic signatures of the exposome-quantifying the impact of exposure to environmental chemicals on human health. *Metabolites* **10**, 454 (2020).
119. Salido, R. A. et al. The International Space Station has a unique and extreme microbial and chemical environment driven by use patterns. *Cell* **188**, 2022–2041.e23 (2025).
120. Calderón, C. & Lämmerhofer, M. Nutritional lipidomics for the characterization of lipids in food. *Adv. Food Nutr. Res.* **105**, 97–172 (2023).
121. Eichelmann, F. et al. Deep lipidomics in human plasma: cardiometabolic disease risk and effect of dietary fat modulation. *Circulation* **146**, 21–35 (2022).
122. Yoo, W. et al. High-fat diet-induced colonocyte dysfunction escalates microbiota-derived trimethylamine N-oxide. *Science* **373**, 813–818 (2021).
123. Forouhi, N. G., Krauss, R. M., Taubes, G. & Willett, W. Dietary fat and cardiometabolic health: evidence, controversies, and consensus for guidance. *BMJ* **361**, k2139 (2018).
124. Tietel, Z. et al. An overview of food lipids toward food lipidomics. *Compr. Rev. Food Sci. Food Saf.* **22**, 4302–4354 (2023).
125. Matsuzawa, Y. et al. Food lipidomics for 155 agricultural plant products. *J. Agric. Food Chem.* **69**, 8981–8990 (2021).
126. Mahrous, E., Chen, R., Zhao, C. & Farag, M. A. Lipidomics in food quality and authentication: a comprehensive review of novel trends and applications using chromatographic and spectroscopic techniques. *Crit. Rev. Food Sci. Nutr.* **64**, 9058–9081 (2024).
127. Kang, J. & Yeo, J. Critical overview of mass spectrometry-based lipidomics approach for evaluating lipid oxidation in foods. *Food Sci. Biotechnol.* **34**, 837–849 (2025).
128. Zhang, H. et al. Integrating widely targeted and oxylipin-targeted lipidomics unravels lipid characteristic evolution and oxidation markers in walnuts during deterioration. *Food Chem.* **466**, 142197 (2025).
129. Zhang, D., Li, X., Duan, X., Sun, H. & Cao, Y. Lipidomics reveals the changes in lipid profile of flaxseed oil affected by roasting. *Food Chem.* **364**, 130431 (2021).
130. Robson, K., Birse, N., Chevallier, O. & Elliott, C. Metabolomic profiling to detect different forms of beef fraud using rapid evaporative ionisation mass spectrometry (REIMS). *NPJ Sci. Food* **6**, 9 (2022).
131. Sazzad, M. A., Al, Fabritius, M., Boström, P. & Yang, B. Advanced tandem mass spectrometric analysis of complex mixtures of triacylglycerol regioisomers: a case study of bovine milk fat. *J. Agric. Food Chem.* **72**, 8849–8858 (2024).
132. Fabritius, M. et al. Direct inlet negative ion chemical ionization tandem mass spectrometric analysis of triacylglycerol regioisomers in human milk and infant formulas. *Food Chem.* **328**, 126991 (2020).
133. Koch, E., Wiebel, M., Löwen, A., Willenberg, I. & Schebb, N. H. Characterization of the oxylipin pattern and other fatty acid oxidation products in freshly pressed and stored plant oils. *J. Agric. Food Chem.* **70**, 12935–12945 (2022).
134. Brejchova, K. et al. Triacylglycerols containing branched palmitic acid ester of hydroxystearic acid (PAHSA) are present in the breast milk and hydrolyzed by carboxyl ester lipase. *Food Chem.* **388**, 132983 (2022).
135. McKillop, K., Harnly, J., Pehrsson, P., Fukagawa, N. & Finley, J. FoodData Central, USDA's updated approach to food composition data systems. *Curr. Dev. Nutr.* **5**, 596 (2021).
136. Barabási, A.-L., Menichetti, G. & Loscalzo, J. The unmapped chemical complexity of our diet. *Nat. Food* **1**, 33–37 (2019).
137. Ruskovska, T., Postolov, F. & Milenkovic, D. Integrated analysis of genomic and genome-wide association studies identified candidate genes for nutrigenetic studies in flavonoids and vascular health: path to precision nutrition for (Poly)phenols. *Nutrients* **16**, 1362 (2024).
138. Eichelmann, F. et al. Lipidome changes due to improved dietary fat quality inform cardiometabolic risk reduction and precision nutrition. *Nat. Med.* **30**, 2867–2877 (2024).
139. Bajželj, B., Laguzzi, F. & Röös, E. The role of fats in the transition to sustainable diets. *Lancet Planet. Health* **5**, e644–e653 (2021).
140. Tzompa-Sosa, D. A. et al. Lipidome of cricket species used as food. *Food Chem.* **349**, 129077 (2021).
141. Alhattab, M., Moorthy, L. S., Patel, D., Franco, C. M. M. & Puri, M. Oleaginous microbial lipids' potential in the prevention and treatment of neurological disorders. *Mar. Drugs* **22**, 80(2024).
142. Justice, I., Kiesel, P., Safronova, N., von Appen, A. & Saenz, J. P. A tuneable minimal cell membrane reveals that two lipid species suffice for life. *Nat. Commun.* **15**, 9679 (2024).
143. Caforio, A. et al. Converting Escherichia coli into an archaebacterium with a hybrid heterochiral membrane. *Proc. Natl. Acad. Sci. USA.* **115**, 3704–3709 (2018).
144. Villanueva, L. et al. Bridging the membrane lipid divide: bacteria of the FCB group superphylum have the potential to synthesize archaeal ether lipids. *ISME J.* **15**, 168–182 (2021).
145. Villanueva, L., Schouten, S. & Damsté, J. S. S. Phylogenomic analysis of lipid biosynthetic genes of Archaea shed light on the 'lipid divide'. *Environ. Microbiol.* **19**, 54–69 (2017).
146. Oemer, G. et al. Molecular structural diversity of mitochondrial cardiolipins. *Proc. Natl. Acad. Sci. USA.* **115**, 4158–4163 (2018).
147. Jouhet, J. et al. Plant and algal lipidomes: analysis, composition, and their societal significance. *Prog. Lipid Res.* **96**, 101290 (2024).
148. Boland, S. et al. Phosphorylated glycosphingolipids essential for cholesterol mobilization in Caenorhabditis elegans. *Nat. Chem. Biol.* **13**, 647–654 (2017).
149. Ng, E. Z. Q., Lee, E., Chng, S.-S., Kim, J. & Guan, X. L. Endogenous formation of phosphatidylhomoserine in Escherichia coli through phosphatidylserine synthase. *J. Biol. Chem.* **301**, 110255 (2025).
150. Surma, M. A. et al. Mouse lipidomics reveals inherent flexibility of a mammalian lipidome. *Sci. Rep.* **11**, 19364 (2021).
151. Linke, V. et al. A large-scale genome-lipid association map guides lipid identification. *Nat. Metab.* **2**, 1149–1162 (2020).
152. Olzhabaev, T., Müller, L., Krause, D., Schwudke, D. & Torda, A. E. Lipidome visualisation, comparison, and analysis in a vector space. *PLoS Comput. Biol.* **21**, e1012892 (2025).
153. Marella, C., Torda, A. E. & Schwudke, D. The LUX Score: a Metric for Lipidome Homology. *PLoS Comput. Biol.* **11**, e1004511 (2015).
154. Guan, X. L. et al. LipidA-IDER to explore the global lipid a repertoire of drug-resistant gram-negative bacteria. *Anal. Chem.* **95**, 602–611 (2023).
155. Zuffa, S. et al. microbeMASST: a taxonomically informed mass spectrometry search tool for microbial metabolomics data. *Nat. Microbiol.* **9**, 336–345 (2024).
156. Gomes, P. W. P. et al. plantMASST - Community-driven chemotaxonomic digitization of plants. *bioRxiv* https://doi.org/10.1101/2024.05.13.593988 (2024).
157. Kelly, J. & Scheibling, R. Fatty acids as dietary tracers in benthic food webs. *Mar. Ecol. Prog. Ser.* **446**, 1–22 (2012).
158. Kühn, J., Henning, V. & Ruess, L. Improving the application of quantitative fatty acid signature analysis in soil food webs: The effects of diet fat content. *Ecol. Evol.* **11**, 11065–11076 (2021).

159. Remili, A. et al. Validation of quantitative fatty acid signature analysis for estimating the diet composition of free-ranging killer whales. *Sci. Rep.* **12**, 7938 (2022).
160. Galloway, A. W. E. et al. A fatty acid based bayesian approach for inferring diet in aquatic consumers. *PLoS One* **10**, e0129723 (2015).
161. Iverson, S. J., Field, C., Don Bowen, W. & Blanchard, W. Quantitative fatty acid signature analysis: a new method of estimating predator diets. *Ecol. Monogr.* **74**, 211–235 (2004).
162. Trautenberg, L. C., Brankatschk, M., Shevchenko, A., Wigby, S. & Reinhardt, K. Ecological lipidology. *Elife* **11**, e79288 (2022).
163. Los, D. A. & Leusenko, A. V. 50 years since the concept of homeoviscous adaptation. *Biochimie* **231**, 98–103 (2025).
164. Winnikoff, J. R. et al. Homeocurvature adaptation of phospholipids to pressure in deep-sea invertebrates. *Science* **384**, 1482–1488 (2024).
165. Holm, H. C. et al. Global ocean lipidomes show a universal relationship between temperature and lipid unsaturation. *Science* **376**, 1487–1491 (2022).
166. Sunagawa, S. et al. Tara Oceans: towards global ocean ecosystems biology. *Nat. Rev. Microbiol.* **18**, 428–445 (2020).
167. Kühn, J., Schweitzer, K. & Ruess, L. Diversity and specificity of lipid patterns in basal soil food web resources. *PLoS One* **14**, e0221102 (2019).
168. Gaud, C. et al. BioPAN: a web-based tool to explore mammalian lipidome metabolic pathways on LIPID MAPS. *F1000Res* **10**, 4 (2021).
169. Rose, T. D. et al. Lipid network and moiety analysis for revealing enzymatic dysregulation and mechanistic alterations from lipidomics data. *Brief. Bioinform.* **24**, bbac572 (2023).
170. Molenaar, M. R. et al. LION/web: a web-based ontology enrichment tool for lipidomic data analysis. *Gigascience* **8**, giz061 (2019).
171. Chen, X.-W. et al. Time for lipid cell biology. *Nat. Cell Biol.* **27**, 169–174 (2025).
172. Symons, J. L. et al. Lipidomic atlas of mammalian cell membranes reveals hierarchical variation induced by culture conditions, subcellular membranes, and cell lineages. *Soft Matter* **17**, 288–297 (2021).
173. Feringa, F. M. et al. The Neurolipid Atlas: a lipidomics resource for neurodegenerative diseases uncovers cholesterol as a regulator of astrocyte reactivity impaired by ApoE4. *bioRxiv* https://doi.org/10.1101/2024.07.01.601474 (2024).
174. Wieder, C. et al. PathIntegrate: multivariate modelling approaches for pathway-based multi-omics data integration. *PLoS Comput. Biol.* **20**, e1011814 (2024).
175. Olivier-Jimenez, D. et al. iSODA: a comprehensive tool for integrative omics data analysis in single- and multi-omics experiments. *Anal. Chem.* **97**, 2689–2697 (2025).
176. Ewald, J. D. et al. Web-based multi-omics integration using the Analyst software suite. *Nat. Protoc.* **19**, 1467–1497 (2024).
177. Menzel, J. P. et al. Ozone-enabled fatty acid discovery reveals unexpected diversity in the human lipidome. *Nat. Commun.* **14**, 3940 (2023).
178. Unfried, M. et al. Lipid Aging Clocks as predictive and prognostic biomarker in cancer and inflammaging. Preprint at https://doi.org/10.1101/2024.09.03.24311998 (2024).
179. Kishimoto, K., Urade, R., Ogawa, T. & Moriyama, T. Nondestructive quantification of neutral lipids by thin-layer chromatography and laser-fluorescent scanning: suitable methods for 'lipidome' analysis. *Biochem. Biophys. Res. Commun.* **281**, 657–662 (2001).
180. Han, X. & Gross, R. W. Global analyses of cellular lipidomes directly from crude extracts of biological samples by ESI mass spectrometry: a bridge to lipidomics. *J. Lipid Res.* **44**, 1071–1079 (2003).
181. Chappel, J. R., Kirkwood-Donelson, K. I., Reif, D. M. & Baker, E. S. From big data to big insights: statistical and bioinformatic approaches for exploring the lipidome. *Anal. Bioanal. Chem.* **416**, 2189–2202 (2024).
182. Salihovic, S., Lamichane, S., Hyötyläinen, T. & Orešič, M. Recent advances towards mass spectrometry-based clinical lipidomics. *Curr. Opin. Chem. Biol.* **76**, 102370 (2023).
183. O'Donnell, B. V. Lipidomics moves to center stage of biomedicine. *Funct. (Oxf.)* **4**, zqac071 (2023).
184. Edwards, B. R. Lipid biogeochemistry and modern lipidomic techniques. *Ann. Rev. Mar. Sci.* **15**, 485–508 (2023).
185. Vriens, K. et al. Evidence for an alternative fatty acid desaturation pathway increasing cancer plasticity. *Nature* **566**, 403–406 (2019).
186. Summers, S. A. Could ceramides become the new cholesterol? *Cell Metab.* **27**, 276–280 (2018).
187. Brocks, J. J. et al. Lost world of complex life and the late rise of the eukaryotic crown. *Nature* **618**, 767–773 (2023).
188. Desmond, E. & Gribaldo, S. Phylogenomics of sterol synthesis: insights into the origin, evolution, and diversity of a key eukaryotic feature. *Genome Biol. Evol.* **1**, 364–381 (2009).
189. Brunoir, T. et al. Common origin of sterol biosynthesis points to a feeding strategy shift in Neoproterozoic animals. *Nat. Commun.* **14**, 7941 (2023).
190. Schebb, N. H. et al. Technical recommendations for analyzing oxylipins by liquid chromatography-mass spectrometry. *Sci. Signal.* **18**, eadw1245 (2025).

Author contributions

The manuscript was conceptualized by M.F. and M.R.D. All the authors were involved in original writing of the sections (Technological Developments in Lipidomics—A.S.; J.B-M.; J.K.; K.S.; M.F.; M.W.; M.R.W; O.F.; P.P.; P.N.; V.O'D.; X.H.; Y.X.; Computational Solutions for Lipidomics—L.G.; M.F.; O.F.; V.O'D.; X.H.; Y.X.; Clinical Lipidomics—A.K.B.; F.G.; J.G.; K.S.; M.H.; M.W.; M.R.W; O.V.; P.M.; Lipidomics in Human Toxicology – C.M.S.; M.O.; Food and Nutritional Lipidomics—B.Y.; L.R.; M.R.D.; Sn.P.; T.R.; Exploring Lipidomes Across the Tree of Life—J.W.; M.R.D.; M.W.; Si. P.; X.L.G.; Lipidomics in Eco-Evo-Devo Research—C.M.S.; A.P.; M.F.; S. Pe.), which was then compiled by M.F., P.P., P.N., V.O'D. and C.M.S.; All authors contributed to the critical revision of the manuscript and approved the final version.

Funding

This publication is based on work from COST Action EpiLipidNET, CA19105, supported by COST (European Cooperation in Science and Technology). M.F. lab is supported by "Sonderzuweisung zur Unterstützung profilbestimmender Struktureinheiten" by the SMWK to TUD, Deutsche Forschungsgemeinschaft (FE 1236/5-1; FE 1236/8-1; TRR 412/1 – 535081457), and Bundesministerium für Forschung, Technologie und Raumfahrt (031L0315A, DEEP_HCC; 01EJ2205A, FERROPath). M.H. acknowledges the support of ERC Adv grant No. 101095860. M.Witting acknowledges funding by The European Union Horizon 2020, Marie Curie Actions, grant number 101073062. L.G. acknowledges the support of the Presidenza del Consiglio dei Ministri-Dipartimento per la Coesione Territoriale e per il Sud (CURI project, n. E67G23000200001). J.G. acknowledges the Ministry of Education and Science within the project "Excellence Initiative - Research University". J.B.M acknowledges the support of MetaboHUB infrastructure funded by the Agence Nationale de la Recherche under the France 2030 programme (MetaboHUB ANR-11-INBS-0010; MetEx+ ANR-21-ESRE-0035; MetaboHUB (JVCE) ANR-24-INBS-0012). B.Y. acknowledges the grants of the Research Council of Finland (Decision No. 356891) and Business Finland (Decision No. 1675/31/2023). X.H. acknowledges the partial support of National Institute on Aging grants R01AG061872, R01AG085545, P30AG013319, and P30AG044271. M.R.D. lab is supported by FCT – Fundação para a Ciência e a Tecnologia I.P., under the project/grant UID/50006 + LA/P/0094/2020 (doi.org/10.54499/LA/P/0094/2020 (Centro de Estudos do Ambiente e Mar (CESAM)) and UID/50006 - Laboratório Associado para a Química Verde - Tecnologias e Processos Limpos. J.W. acknowledges the National Institutes of Health (R35GM152060). S. Petrović. acknowledges the support of The Ministry of Science, Technological Development and Innovation of the Republic of Serbia, Contract No. 451-03-136/2025-03/200015. P.P. acknowledges funding by the Deutsche Forschungsgemeinschaft (grant number 565977762). F.G. gratefully acknowledges the financial support of the Federal Ministry of Economy, Energy and Tourism of Austria and the National Foundation for Research, Technology, and Development of Austria to the Christian Doppler Laboratory for Skin Multimodal Imaging of Aging and Senescence.

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to Maria Fedorova or Maria Rosário Domingues.

Peer review information *Nature Communications* thanks Jeremy Koelmel and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

Reprints and permissions information is available at http://www.nature.com/reprints

Maria Fedorova[1] ✉, **Anne K. Bendt**[2], **Justine Bertrand-Michel**[3], **Oliver Fiehn**[4], **Joanna Godzien**[5], **Laura Goracci**[6], **Florian Gruber**[7], **Xue Li Guan**[8,9], **Xianlin Han**[10], **Michal Holčapek**[11], **Julia Kuligowski**[12], **Peter J. Meikle**[13,14], **Palina Nepachalovich**[1], **Valerie B. O'Donnell**[15], **Matej Orešič**[16,17,18], **Sider Penkov**[1], **Snježana Petrović**[19], **Anton Potapov**[20], **Patricia Prabutzki**[21,22], **Laura Righetti**[23], **Tatjana Ruskovska**[24], **Andrej Shevchenko**[25], **Kai Simons**[25,26], **Corinne M. Spickett**[27], **Olga Vvedenskaya**[26], **Jennifer Watts**[28], **Markus R. Wenk**[29], **Michael Witting**[30,31], **Yu Xia**[32], **Baoru Yang**[17] & **Maria Rosário Domingues**[33] ✉

[1]Center of Membrane Biochemistry and Lipid Research, University Hospital Carl Gustav Carus and Faculty of Medicine of TU Dresden, Dresden, Germany. [2]Singapore Lipidomics Incubator, Singapore, Singapore. [3]MetaboHUB-MetaTou, Toulouse, France. [4]West Coast Metabolomics Center, University of California-Davis, Davis, CA, USA. [5]Medical University of Bialystok, Bialystok, Poland. [6]University of Perugia, Perugia, Italy. [7]Department of Dermatology, CDL SKINMAGINE, Medical University of Vienna, Vienna, Austria. [8]Nanyang Technological University, Singapore, Singapore. [9]Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark. [10]The University of Texas Health Science Center at San Antonio, San Antonio, TX, USA. [11]University of Pardubice, Pardubice, Czech Republic. [12]Health Research Institute La Fe (IIS La Fe), Valencia, Spain. [13]Baker Heart and Diabetes Institute, Melbourne, VIC, Australia. [14]Baker Department of Cardiovascular Research, Translation and Implementation, La Trobe University, Melbourne, VIC, Australia. [15]Cardiff University, Cardiff, UK. [16]Örebro University, Örebro, Sweden. [17]University of Turku, Turku, Finland. [18]Åbo Akademi University, Turku, Finland. [19]University of Belgrade, Belgrade, Serbia. [20]Senckenberg Museum for Natural History Görlitz, Görlitz, Germany. [21]Leipzig University, Leipzig, Germany. [22]Maastricht University, Maastricht, Netherlands. [23]Wageningen University & Research, Wageningen, Netherlands. [24]Faculty of Medical Sciences, Goce Delcev University, Stip, North Macedonia. [25]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany. [26]Lipotype GmbH, Dresden, Germany. [27]Aston University & Aston Institute for Membrane Excellence, Birmingham, UK. [28]Washington State University, Pullman, WA, USA. [29]Hamad Bin Khalifa University, Doha, Qatar. [30]Metabolomics and Proteomics Core, Helmholtz Zentrum München GmbH, Neuherberg, Germany. [31]Chair of Analytical Food Chemistry, TUM School of Life Sciences, Technical University of Munich, Freising-Weihenstephan, München, Germany. [32]Tsinghua University, Beijing, China. [33]CESAM- Centre for Environmental and Marine Studies, Department of Chemistry, University of Aveiro, Aveiro, Portugal. ✉e-mail: maria.fedorova@tu-dresden.de; mrd@ua.pt