LIPID MAPS: Powering discovery in lipidomics

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Abstract

As lipidomics approaches its 25th anniversary, we explore how lipid research has matured over the years, while highlighting emerging innovations that are expanding our ability to study these diverse, life-critical biomolecules. In particular, we showcase the community-driven, open-access databases, software, and educational resources made freely available through the ELIXIR Core Data Resource LIPID MAPS for the benefit of both established and new researchers.

Lipid species and their concentrations change in response to internal and external stimuli, serving as valuable indicators of health and disease. About 25 years ago, the advent of benchtop mass spectrometry (MS) drove the emergence of lipidomics, with the LIPID MAPS consortium (www.lipidmaps.org) established to meet the growing need for standardized nomenclature, systematic structural classification, and the organization of experimental data. Here, we provide an update on state-of-the-art innovations in lipidomics, highlighting how LIPID MAPS supports members of the community to apply these new approaches to their own research.

In 2019 (*1*), lipid researchers were anticipating how large-scale, global high-throughput analysis of lipids might contribute to or drive the field of precision medicine. Since then, methods enabling the quantitation of hundreds-to-thousands of lipids driven by innovations in chromatography and MS/MS have revolutionized lipidomics of large cohorts and tissues. Quantification of multiple molecular species across diverse lipid families in a single sample is now robust and becoming more routine, with increased annotation confidence. A lipid-based clinical score for cardiovascular

disease was developed, and stratification of pancreatic cancer was also achieved, using serum or plasma (*2, 3*). Clinical translation of targeted lipidomics has been achieved for some diseases; for example, sphingolipidomics in the screening of newborns for metachromatic leukodystrophy, whereby a sulfatide acts as a biomarker (*4*). Aiming toward translation, NIST-1950 plasma was adopted as reference material, and ring trials for ceramides and bile acids were initiated by the International Lipidomics Society (ILS) and the Singapore Lipidomics Group (SLING), with the latter reporting in 2024 (*5*).

New lipidomics innovations continue to be driven by technological and methodological advances. These include "enhanced fragmentation" achieved by oxygen attachment dissociation (OAD), electron-activated dissociation (EAD), ultraviolet-photodissociation (UV-PD), and ozone-induced dissociation (OzID), which can also determine stereochemistry. These methods generate substantially more structural information than is generated by collision-induced dissociation (CAD/CID), and coupled with high-resolution MS, they greatly increase the molecular diversity of detectable lipids that can be curated. However, we generally lack reference spectra for these "enhanced fragmentation" modalities. A second area of development is molecular networking, whereby data-dependent analysis of globally sourced MS/MS data is expanding the numbers of known lipids, including, for example, new polyamine bile amidates (*6*). Here, a challenge lies in the annotation of species using rule-based approaches unique to lipids. Last, driven by community-agreed needs to support data quality, a substantial focus has been on standardizing lipidomics, by developing the ILS reporting checklist and technical recommendations for oxylipin analysis (*7, 8*), which are aligned with and supported by the data and resources provided by LIPID MAPS.

Working alongside experimental data depositories (Metabolomics Workbench and MetaboLights), small-molecule databases (ChEBI, SwissLipids, and PubChem), and supported by communities contributing data and establishing reporting standards (ILS and EpiLipidNET), LIPID MAPS provides databases, tools, and resources to enable large-scale lipidomics, integration of multi-omics (systems biology), and smaller scale, targeted lipid research. Indicating its size and scale, LIPID MAPS was accessed by >182,000 users in 2025, from almost every country in the world, with >4.1 million pageviews (Fig. 1). In 2024, LIPID MAPS became an ELIXIR Core Data Resource and an ELIXIR Deposition Database and joined the Global Biodata Coalition.

Many lipids from diverse biological sources are not fully structurally characterized and thus remain missing from databases. This is a growing concern, especially with the increasing use of enhanced fragmentation methods, and is particularly relevant for "epilipids," which are modified by enzymatic, non-enzymatic, or environmental factors and are detectable by MS but lack full structural annotation. Although these can be included in resources for molecular networking, such as the Global Natural Products Social Molecular Networking database (GNPS), they often lack structural descriptions. Developed in collaboration with the EU COST Action (CA19105) network EpiLipidNET, the LIPID MAPS database Partial Spectra DB provides >450 annotated and expert-curated MS/MS spectra and associated metadata, including for mammalian neutral glycosphingolipids, microalgal glycosyldiacylglycerols, and bacterial acylaminosugars. Further supporting efforts to structurally identify lipids, ~1800 interactive, downloadable MS/MS spectra for oxylipins and sterols were added to the LIPID MAPS Standards Spectra DB with standardized metadata. Stable identifiers for reporting in publications were provided in a new Shorthand DB to identify lipids described at the species/molecular species levels. Updates to lipid shorthand

nomenclature were implemented, including the expansion of bile acid conjugate notation to include amino acid conjugates using three-letter codes and modifying taurine conjugate notation from ";T" to ";Tau" to eliminate ambiguity.

A large number of new features were added to the LIPID MAPS Structure Database (LMSD) since the last database update (*9*). These include biological information provided by Cayman Chemical for >1500 lipids. LMSD now hosts links from individual lipids to raw data from thousands of lipidomics studies held on Metabolomics Workbench. Links to nuclear magnetic resonance (NMR) spectra (NP-MRD) and MS/MS data on MassBankEU were included. The open-access lipidomics software MS-DIAL 5 incorporated LMSD search functionality, as did Lipostar. LIPID MAPS reached a milestone of 50,000 lipid structures curated in LMSD, including structures discovered by enhanced fragmentation and through molecular networking. LIPID MAPS made available two large archives of historical GC/MS data to aid in the annotation of spectra obtained with this approach. About 1300 steroid spectra generated by Jan Sjövall at the Karolinska Institutet, accompanied by handwritten structural depictions and supplementary notations, were uploaded, whereas a collection of >700 spectra for prostaglandins, leukotrienes, and related fatty acids authored by Cecil Pace-Asciak was reproduced (*10*).

Several new tools have been added to LIPID MAPS, including: (i) a standalone tool enabling the direct calculation and visualization of isotope patterns for user-defined molecular formulae; (ii) an Android version of the Lipid Calculator App, complementing the previously updated iOS application available from LIPID MAPS; (iii) a steroid structure drawing tool that accommodates >20 sterol cores, including steroid hormones, bile acids, and plant sterols; and (iv) a

multifunctional tool enabling the generation of structures for cholesterol esters and many other lipids.

As lipidomics continues to expand in scale, complexity, and clinical relevance, sustained community engagement and data sharing will be essential to ensure that the emerging lipid diversity can be confidently annotated, interpreted, and translated. By evolving in step with new technologies and standards, LIPID MAPS is positioned to remain a central, enabling infrastructure for the next phase of discovery-driven and translational lipidomics.

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Fig. 1. Schematic summarizing updates to the site and the global reach of LIPID MAPS. Usage data were derived from Google Analytics.

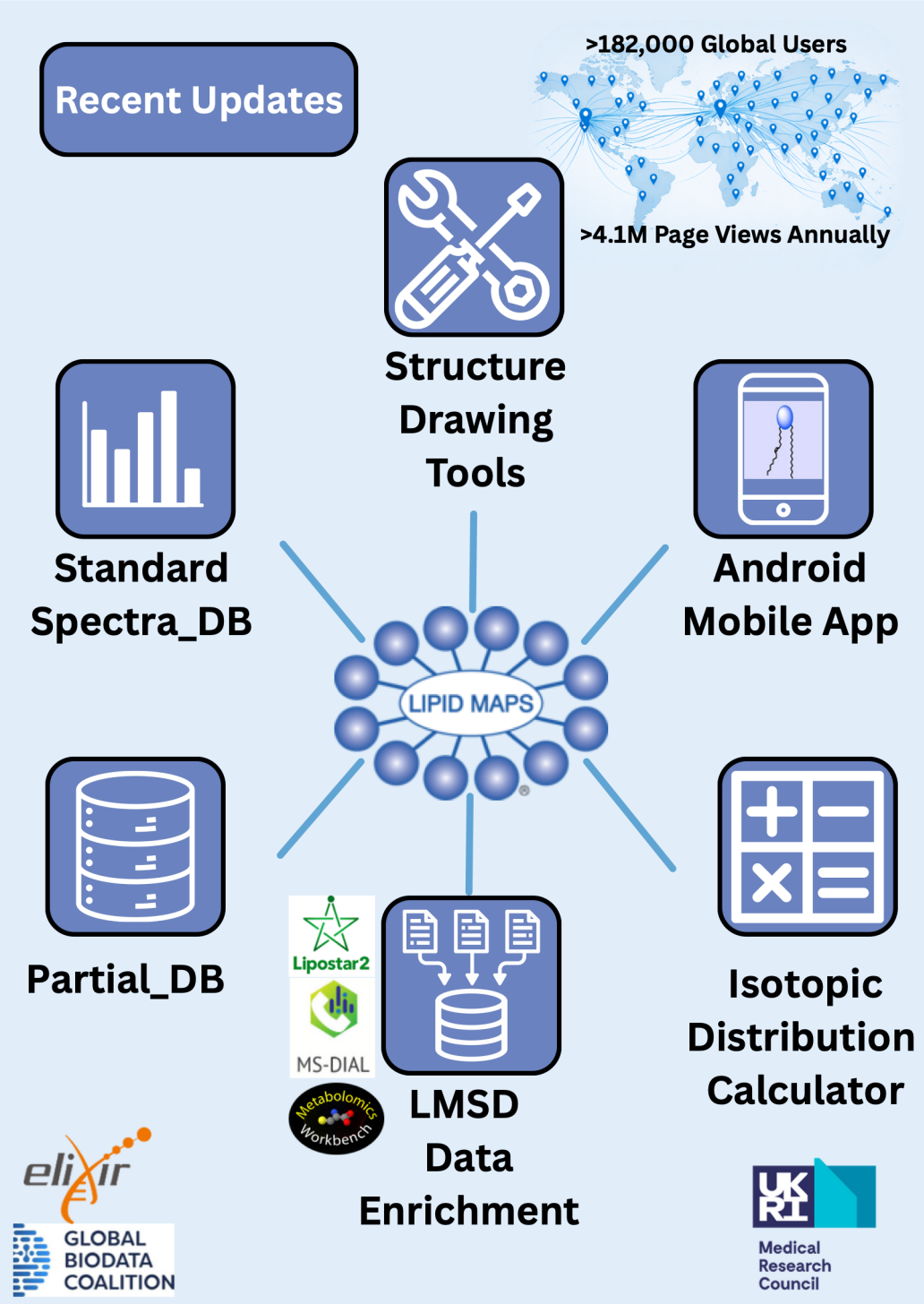

Figure 1. Schematic showing a summary of recent updates and global reach of LIPID MAPS. User figures are from Google Analytics.