Prostaglandins & other Lipid Mediators 128–129 (2017) 8–16

Contents lists available at ScienceDirect

Prostaglandins and Other Lipid Mediators

Review Article

Recent advances in lipidomics: Analytical and clinical perspectives

Sumit Sethi, Elisa Brietzke*

Interdisciplinary Laboratory for Clinical Neuroscience (LiNC), Department of Psychiatry, Universidade Federal de São Paulo - UNIFESP, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 27 July 2016
Received in revised form
22 December 2016
Accepted 22 December 2016
Available online 27 December 2016

Keywords:
Biomarker
Lipid
Lipidomics
Liquid chromatography
Mass spectrometry
Metabolomics

ABSTRACT

Lipidomics or lipid-profiling is a lipid-targeted metabolomics approach aiming at comprehensive analysis of lipids in biological systems. The extent of information in the genomic and proteomic fields is greater than that in the lipidomics field, because of the complex nature of lipids and the limitations of tools for analysis. Modern technological advances in mass spectrometry and chromatography have greatly improved the developments and applications of metabolic profiling of diverse lipids in complex biological samples. Lipidomics will not only provide insights into the specific functions of lipid species in health and disease, but will also identify potential biomarkers for establishing preventive or therapeutic programs for human diseases. In this review, emphasis is given to the current advances in lipidomics technologies and their applications in disease biomarker discovery, and its clinical application. The application of lipidomics in clinical studies may provide new insights into lipid profiling and pathophysiological mechanisms. We also discuss the lipidomics for the future perspectives and their potential problems.

Contents

Abbreviations: CE, cholesteryl ester; DI, direct infusion; ESI, electrospray ionization; FA, fatty acyl; FFA, free fatty acid; GC, gas chromatography; GL, glycerolipid; GP, gycerophospholipid; MSI, mass spectrometry imaging; IM, ion mobility; LC, liquid chromatography; MS, mass spectrometry; MALDI, matrix-assisted laser desorption/ionization; NMR, nuclear magnetic resonance; PL, phospholipid; SPE, solid-phase extraction; SP, sphingolipid; TLC, thin layer chromatography; TOF, time-of-flight; UPLC, ultra-performance liquid chromatography.

* Corresponding author at: Interdisciplinary Laboratory for Clinical Neuroscience (LiNC), Department of Psychiatry, Universidade Federal de São Paulo - UNIFESP, Research Building II, Rua Pedro de Toledo, 669-3 Floor Funds - Vila Clementino, São Paulo, Brazil.
E-mail address: elisabrietzke@hotmail.com (E. Brietzke).

http://dx.doi.org/10.1016/j.prostaglandins.2016.12.002
1098-8823/

1. Introduction

Lipidomics can be defined as the large-scale study of lipid species and their related networks and metabolic pathways that exist in cells or any other biologic system. The goal of this "-omics" is the full characterization, identification, and quantification of molecular lipid species and their biologic roles regarding the expression of proteins involved in lipid metabolism and function, including gene regulation. As an emerging "-omics" field, lipidomics provides a powerful approach to understanding lipid biology. Recently, it has been widely renowned that lipids are central to the regulation and control of cellular function and disease [1]. Therefore, lipidomics has gained a lot of consideration and become an emerging field of basic and translational research.

Lipids, the fundamental components of biologic membranes, are a structurally and functionally diverse class of molecules. Depending on biosynthesis and chemical structure, lipids are defined as hydrophobic or amphiphilic. Amphiphilic lipids exist in vesicles, membranes, or liposomes in an aqueous environment. Biologic lipids originate two distinct types of biochemical subunits: isoprene and ketoacyl groups. Based on this definition, lipids can be divided into eight categories: fatty acyls (FAs), glycerolipids (GLs), sphingolipids (SPs), glycerophospholipids (GPs), saccharolipids (SLs), sterol lipids (ST), prenol lipids (PR), and polyketides (PK) (Fig. 1). The large amount of categories and the extremely complex structures of lipids lead to a formidable challenge to fully analyze all lipids. Nowadays, there are two strategies to analyze lipids: targeted lipids analysis and non-targeted lipid analysis. The targeted lipids analysis emphases on known lipids, and develops a specific method with a high sensitivity for the quantitative analysis of these specific lipids. Non-targeted lipids analysis aims to identify every lipid species concurrently. In order to successfully realize the qualitative and quantitative analysis of lipids, many analytical methods have been established for the analysis of lipids, including thin-layer chromatography (TLC), gas chromatography (GC), and mass spectrometry (MS). Especially the development of "soft" ionization techniques as electrospray ionization (ESI) and exact mass resolution, high resolution mass spectrometers have greatly propelled the field of lipidomics. In addition, new bioinformatics tools have been developed to cope with the increasing amounts of raw data and extract relevant information to yield biological insight. Taken together, lipid analysis needs a serial of methods and technologies, including lipid extraction methods, MS-based analytical technologies and bioinformatics tools. A flowchart of the study of lipidomics is shown in Fig. 2.

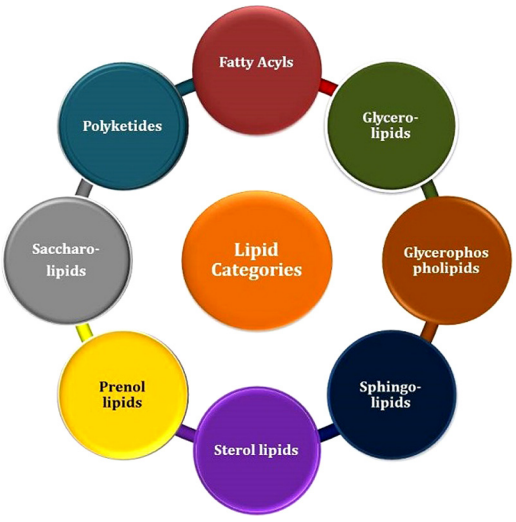

Fig. 1. Schematic representation of different lipid classes.

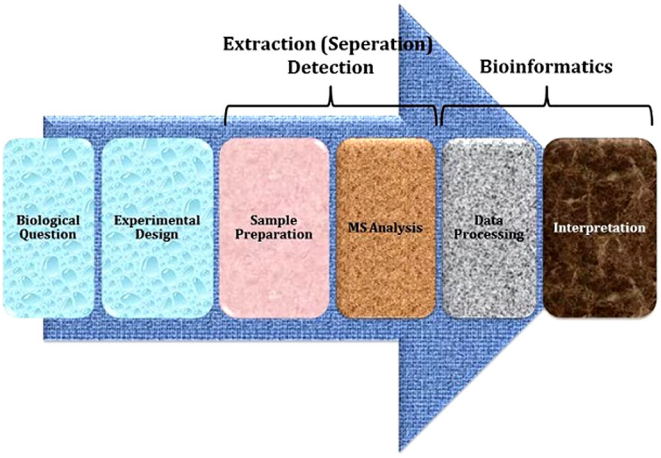

Fig. 2. Workflow summarizing the different steps in lipidomics analysis.

Lipidomics will not only provide insights into the specific functions of lipid species in health and disease, but will also identify potential biomarkers for establishing preventive or therapeutic programs for human diseases [2]. Lipid-based biomarkers offer new opportunities for precision medicine by providing sensitive diagnostic tools for disease prediction and monitoring. This review article emphasis the recent developments in lipidomics technologies and their applications in disease biomarker discovery, and discuss the lipidomics for the future perspectives. The application of lipidomics in clinical studies may provide new insights into lipid profiling and pathophysiological mechanisms.

2. Sample preparation and lipid extraction

It is known that manual lipid extraction is labor-intensive and prone to errors thereby prohibiting the large scale studies containing hundreds or thousands of samples. Automation of the sample preparation and extraction process is therefore required for large scale lipidomics studies. Automation has the surplus advantage of significantly improving the study cost-effectiveness. The process should be accomplished such that no artifacts will be made while maintaining the endogenous lipids intact. Suitable assortment of solvents, reagents, sample amounts, lipid standards, hardware, and protocols should be carefully considered since all components of the process will influence the quality of the final lipidomic dataset.

Typically, 5–100 μL of biofluids (plasma or serum) or 1–100 mg of tissue per analysis is essential for lipidomic analyses for global profiling. The most common method for the extraction of lipids is based on liquid extraction. The solubility of lipids in organic solvents is controlled by the hydrophobic hydrocarbon chains of the fatty acid or other aliphatic moieties and any polar functional groups, such as phosphate or sugar residues, which are markedly hydrophilic. Triacylglycerols (TGs), and cholesteryl esters (CEs) are neutral lipids that do not have any polar groups, and are thus readily soluble in nonpolar solvents (e.g., hexane, toluene, or cyclohexane) and also in moderately polar solvents (e.g., diethyl ether or chloroform), whereas they have relatively low solubility in polar solvents such as methanol. More polar lipids such as phospholipids (PLs) and SPs are only slightly soluble in hydrocarbon-based solvents, but they have good solubility in more polar solvents such as methanol, ethanol, and chloroform. The pH is also important in the extraction of specific lipid subclasses, either because of their acid-base characteristics or because of degradation at specific pH environments. For example, acidic lipids such as phosphatidic acid