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REVIEW

Advance in Analysis and Detection Technologies for Phospholipidomics

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Abstract: Phospholipids, the principal constituents of cell membranes, has very important physiological functions and is closely related to human health and diseases. Therefore, comprehensive analysis of phospholipids is essential to enhance our understanding of function of phospholipids in disease process. Phospholipidomics is a phospholipids-targeted metabolomic approach which focuses on comprehensive qualitation and quantitation of phospholipids in biological system. Phospholipidomics study is carried out by the analysis and detection techniques involved in sample preparation, separation, qualitation and quantitation and data mining. In this paper, the analysis and detection methods for phospholipidomics are reviewed, providing a valuable reference for developing stable, reliable, high sensitivity, high resolution and high throughput platform techniques for phospholipidomics. The integrated investigation of phospholipidomics and other omics is proposed to promote the further development of analytical bioscience.

Key Words: Phospholipids; Analysis; Phospholipidomics; Review

1 Introduction

Phospholipids (PLs), the principal constituents of cell membranes, are the bioactive substance and the storage materials of signal molecular precursor, and play very important roles in cell growth, cell migration, cellular signal transduction, cell recognition, cell interaction and cell apoptosis[1–9]. Phospholipids can regulate the metabolism process due to their ability to affect the endocrine and nervous system, and thus some of PLs are considered as the potential biomarkers associated with obesity, diabetes, cancer, Alzheimer's disease, cardiovascular disease, etc[10–16]. Therefore, an accurate and efficient detection of PLs in biosamples is essential to investigate the relationship between the PLs and the disease process and biological functions of PLs in disease prevention, diagnosis and treatment.

Phospholipidomics focuses on comprehensive qualitation and quantitation of phospholipids in biological system so as to solve biological problems associated with PLs and their metabolism. As shown in Fig.1, the phospholipidomic strategy is to propose the solution to the biological problems firstly, including the disease occurrence, development, diagnosis, treatment, and safety and the efficacy evaluation of drugs, then to design and implement the experimentation during which all data of the measured samples are processed by multivariate statistical analysis to discover the related potential biomarkers, so as to process biomarker validation and biological interpretation. The stable data are required for phospholipidomics.

The analysis and detection techniques for phospholipidomics

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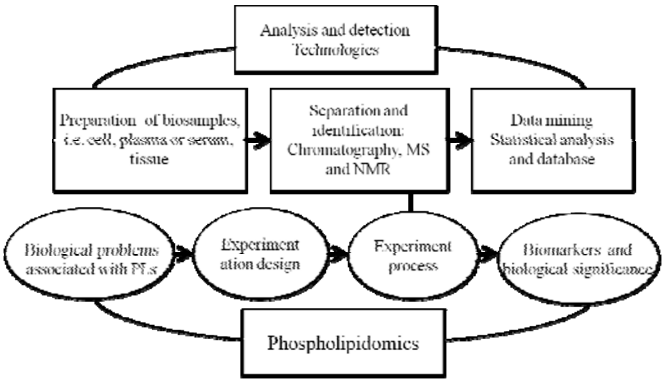

Fig.1 Strategy for phospholipidomics

refer to sample preparation, PLs separation, qualitation and quantitation analysis, data mining and database construction. In this paper, the analysis and detection techniques for phospholipidomics are reviewed and a valuable reference is provided for developing stable, reliable, high throughput platforms.

2 Classes and structure of PLs

PLs mainly include glycerophospholipids and sphingomyelin. A glycerophospholipid molecule (Fig.2A) is consisted of phosphoric group, glycerol group, head group (hydrophilic) and tail group (hydrophobic). The classification of PLs depends on the different head groups such as choline, ethanol amine, inositol, serine, glycerol, etc. Glycerophospholipids mainly contains phosphatidic acid (PA), lysophosphatidic acid (LPA), phosphatidylcholine (PC), lysophosphatidylcholine (LPC), phosphatidylethanolamine (PE), lysophosphatidylethanolamine (LPE), phosphatidylinositol (PI), lysophosphatidylinositol (LPI), phosphatidylserine (PS), lysophosphatidylserine (LPS), phosphatidylglycerol (PG), lysophosphatidylglycerol (LPG), diphosphatidylglycerol (DPG) and so on. The hydrophobic tails are non polar end containing one or two fatty acid chains with different carbon number (n = 14–22) and different unsaturated degree (n = 0–6). Usually, saturated fatty acid chain is at position C1 of glycerol group and unsaturated chain at position C2.

As shown in Fig.2B, the structure of sphingomyelin is similar with glycerophospholipids, containing phosphoric group, sphingol group, head group (hydrophilic) and tail group (hydrophobic). The polar head group R' may be choline and ethanol amine while the non polar tail group is consisted of one unsaturated fatty acid chain and an alkyl chain. Some of isomers of PLs have fatty acid chains with the same carbon number and unsaturated degree but different C=C location. According to the differences of tail group, there are various species in the same PLs class. And theoretically more than 1000 PLs compounds could be identified.

PLs are amphiphilic molecules. The primary mission of the

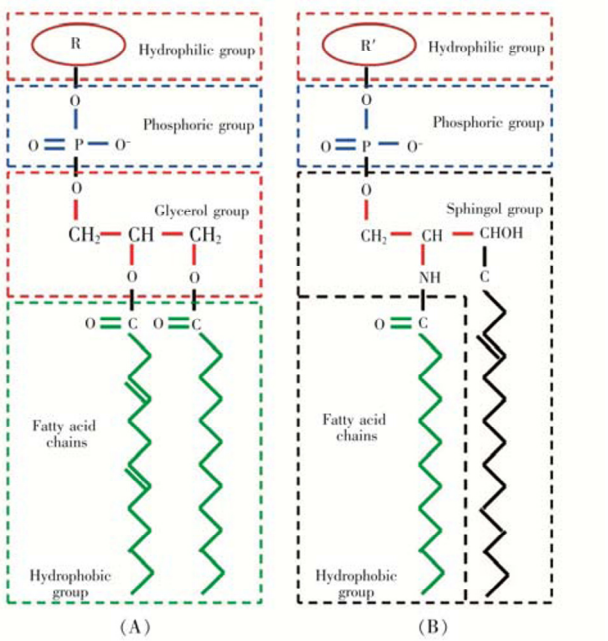

Fig.2 Molecular structure of phospholipids: (A) Glycerol phospholipid; (B) Sphingomyelin

analysis and detection techniques for PLs is to obtain qualitative and quantitative data for screening potential biomarkers, so as to create an efficient database. With the development of instrumental analysis and computational science, a novel platform technique based on combination of different methods is important in satisfying the requirements to develop a simple and rapid method with high sensitivity, high resolution and high throughput for systematic analysis of PLs.

3 Analysis and detection techniques

3.1 Preparation of bio-samples

3.1.1 PLs extraction

PLs in diverse biological samples[17] such as plasma, serum, tissue and cell need to be measured for phospholipidomics. The often used methods for extracting PLs from complex biological sample include liquid-liquid extraction, solid phase extraction and single solvent extraction.

During last decade, many liquid-liquid extraction methods were reported, such as Folch method[18,19,22], Bligh and Dyer (BD) mrthod[19,20], Gerber method[21], Babcock method[21], Werner-Schmid method[21], and Rose-Gottlieb method[22]. Among them, BD method is considered as “golden standard” for lipid extraction, in which methanol and chloroform were used as extract solvent to get wide-range and high efficiency extraction. BD method is widely applied to total lipid extraction of cell, plasma, brain tissue and liver tissue[23–25]. Hexane/isopropanol/acetone is another commonly used extract