Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Biotechnology

Using lipidomics analysis to determine signalling and metabolic changes in cells

An Nguyen, Simon A Rudge, Qifeng Zhang and Michael JO Wakelam

Recent advances in lipidomics tools and software assist in the identification and quantification of lipid species detected by mass spectrometry. By integrating mass spectrometric lipid data into mapped pathways and databases, an entire network of lipid species which both demonstrates the complexity of lipid structures and biochemical interactions can be constructed. Here we demonstrate lipidomics analysis at both systematic and molecular levels. This review focuses on four points: how lipid data can be collected and processed with the support of tools, software and databases; how lipidomic analysis is performed at the molecular level; how to integrate data analysis into a biological context; how the results of such analysis predict enzyme activities and potential sites for therapeutic interventions or manipulation of enzyme activities.

Address
The Babraham Institute, Babraham Research Campus, Cambridge CB22 3AT, United Kingdom

Corresponding author: Wakelam, Michael JO (Michael.wakelam@babraham.ac.uk)

Current Opinion in Biotechnology 2017, **43**:96–103

This review comes from a themed issue on **Analytical biotechnology**

Edited by **Jurre Kamphorst** and **Ian Lewis**

http://dx.doi.org/10.1016/j.copbio.2016.10.003

0958-1669/© 2016 Elsevier Ltd. All rights reserved.

Introduction

Lipids are a group of distinct biological molecules that can be subdivided into neutral lipids such as fatty acids, mono- di- and triacylglycerols (MG, DG and TG); phospholipids including cardiolipin (CL), phosphatidylcholine (PC), phosphatidylethanolamine (PE) and phosphatidylinositol (PI); sphingolipids, such as sphingomyelin (SM), ceramide (Cer) and sphingosine-1-phosphate (S1P); sterols and prenols, polyketides and saccharolipids. Each class of lipids has the potential to comprise a variety of molecular species differing in acyl carbon chain length as well as in the position and number of double bonds, thereby accounting for much of the lipid diversity. It has been approximated that there are about 10,000 lipid species in mammalian cells [1•]. Lipids are cellular building blocks, and thus this diversity in structure will impact the biophysical properties of cellular membranes. Moreover, a number of lipids participate in various different biological processes including functioning as signalling intermediates, (e.g. diacylglycerol as an activator of protein kinase C), and as binding partners selectively docking proteins to membranes (such as phosphatidylinositiol 3,4,5-trisphosphate (PIP_3) interacting with PH domains in proteins [2]). Consequently, alterations in lipid structure, including acyl carbon chain length and number of double bonds, could alter membrane structure and therefore induce changes in dynamic activities of cellular membranes. For instance, short-chained and saturated lipids generate a more tightly packed and compressed cell membrane whilst, in contrast, longer-chained and unsaturated lipids occupy more space and are more mobile in membranes, thereby increasing fluidity and providing greater opportunities for lipids and proteins to interact. Consequently, such alterations in lipid structure and membrane dynamic properties will affect both metabolic and signalling functions of cell membranes. In addition, longer and more unsaturated acyl chain lipids can spread and bend; which has the potential to make the lipid bilayers thinner and permeable to water and other small molecules. As a result of this, not only are lipids directly involved in many important complex biological processes, but they can also impact other processes leading to critical changes in cellular membrane functions. For this reason, it is recognized that it is important for lipidomics analysis to be carried out in order to understand how changes in lipids affect metabolic and signalling pathways. The following sections will outline how this can be performed in lipid species analysis and pathway analysis.

Tools for lipid interpretation

In lipidomics, lipid species are identified and quantified by liquid chromatography–mass spectrometry (LC- or HPLC-MS), with detailed structural identification being based upon both accurate mass determination and fragmentation. The need for standardization of data generated by all lipidomics laboratories lead to a standardized nomenclature being developed [3,4]. As mass spectrometers have become more accurate and sensitive, the analysis of individual molecular species based on their mass-to-charge ratio has become more accurate. Nevertheless, the continued use of mass spectrometers with varying degrees of resolution often results in incorrect

structural assignments. To address this we have defined a methodology that takes into account the distinct degrees of structural definition that can be achieved with different resolutions and have determined an appropriate nomenclature [5•] which builds upon that of LIPID MAPS and its tools [6]. As an example, PC(O-16:0/18:1(9Z)) and PC(O-18:0/16:1(9Z)) have identical molecular masses of 745.60 and can only be distinguished full fragmentation, whilst a less sensitive MS might additionally confuse these lipids with PC(15:0/18:1(11Z)) or PC(16:0/17:1(9Z)) which both have a molecular mass of 745.56 (see Ref. [5•] for further discussion). Lipidomics is distinct from proteomics in that the range of masses is smaller. In addition, each lipid class contains many distinct molecular species that sometimes only differ in the presence or absence of a single double bond. Nevertheless, the process of analyzing mass spectrometric lipidomics data has been supported by several software packages and tools, a number of these are reviewed in [7]. The purpose of these is to, where possible, automate the characterization and quantification of a complex lipidome through interpretation of large mass spectra datasets. As a result, this process allows identification of structures of molecular lipid species. There are a number of web-based lipid databases including LipidMaps (http://lipidmaps.org), LipidBank (http://lipidbank.jp), LipidHome (http://www.ebi.ac.uk/metabolights/lipidhome/) and LipidSearch (http://lipidsearch.jp) that include information about molecular structures and mass spectra. These web services are appropriate for distinct purposes. For example, LipidMaps, funded by the National Institutes of Health and the National Institute of General Medical Sciences, has been developed with aims to build an integrated system for characterizing the global changes in lipid metabolites [8]. This allows the drawing of lipid structures whilst also assisting in the prediction of potential structures from mass spectrometry data [6]. Another useful utility is text-based search, allowing users to enter a lipid name or synonym, mass or molecular formula in search form, the results being displayed in tabular format together with detailed information of each molecule. Apart from traditional text/ontology-based search, a structure-based search has been also developed in order to search for lipid species based on structure of lipid drawn by users. Users can also utilize one of three structure drawing tools such as MarvinSketch (https://www.chemaxon.com), JME (http://jmol.sourceforge.net) and ChemDrawPro (http://www.cambridgesoft.com/). MarvinSketch and JME are Java applet based tools which require only an applet supported browser to be able use, ChemDrawPro is a desktop application that enables users to effectively draw molecules, reactions, pathways as well as exploring structure activity relationships.

LipidBank is an official database of the Japanese Conference on the Biochemistry of Lipids (JCBL) which covers more than 7000 distinct species, this can be linked to LipidSearch. This software developed by Professor Ryo Taguchi and MKI, (Tokyo, Japan), is an identification tool for cellular lipid molecular species defined by experimental mass data [9,10]. The EBI (European Bioinformatics Institute) has released the first version of LipidHome which enables users to search for either masses of lipids by name or lipid species by a list of defined precusor ion masses [11]. Whilst this tool only provides data for glycerolipids and glycerophospholipids, it allows users to download a group of found lipid species with masses in different formats (csv, excel, etc.) which may be useful for programmatic purposes (such as calculation of molecular concentrations). Additionally, another search tool, lipID, is also provided to help users search for possible lipid species given masses or mass–charge ratios [12]. There are also tools that can process and display data in pseudo-3D format, such as SECD (Spectrum Extraction from Chromatographic Data), in which MS raw data is used as an input for the extraction of mass spectra before being processed for display. The data obtained from this can then be used as an input for another tool entitled LIMSA (Lipid Mass Spectrum Analysis), which identifies and quantifies lipid species for further processing. This tool also provides a convenient graphic user interface with many options for users to choose from, such as setting parameters to use for analysis or finding peaks for searching lists of pre-defined compounds [13].

Advances in mass spectrometer technologies, that increasingly acquire both MS and MS/MS data, have prompted further software development. An example of this is Lipid-Pro, which enables lipid identification from data-independent acquisition from tandem MS [14]. Lipid Data Analyser (LDA) further recognizes the need for MS platform-independence in enabling data from different laboratories to be compared and integrated. In LDA lipid annotation is based on both defined fragments and intensity relationships facilitating routine profiling of known lipid targets and the detection of novel lipids (http://genome.tugraz.at/lda/lda_description.shtml). Even though these tools enable lipid classification, identification and quantification of information, that are essential for the study of lipids at a system level, they fail to provide a deeper insight into the more complex biological context at a molecular level. A number of studies have attempted to mine lipidomics data to understand physiological changes, for example Slatter *et al.* found that fatty acids and oxidized species support energy generation in human platelets. In addition, this study pointed to the presence of multiple unidentified lipid species [15••]. Whilst this study clearly pointed to activation of $cPLA_2$ in the platelets, it is probable that this was not the only lipid metabolism or signalling pathway activated. A fruitful area has been examining the effects of viral infection upon cellular lipidomes, Gaunt *et al.* [16] found that rotavirus infection significantly modified lipid droplet-associated lipids whilst Tam *et al.* [17] demonstrated that influenza infection induced a significant

Download English Version:

https://daneshyari.com/en/article/6487365

Download Persian Version:

https://daneshyari.com/article/6487365

Daneshyari.com