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Handbook of Neurochemistry and Molecular Neurobiology

3rd Edition

Neural Lipids

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Abel Lajtha (Ed.)

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Volume Editors: Guido Tettamanti and Gianfrancesco Goracci

With 120 Figures and 56 Tables

Springer

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Preface

The second Edition of the "Handbook of Neurochemistry" goes back to 1983. In that Edition, Brain lipids were distributed in different volumes, following the rationale underlying the Edition. Many of the chapters on lipids were outstanding and actually are "historical masterpieces" of scientific literature. After more then 25 years, the lipids of the nervous system were considered to deserve a separate volume. Many are the reasons for this decision. New methods have been developed for the structural analysis of lipids, for their quantification at the nano and pico mole levels, for the synthesis of analogs and derivatives suitable for biological investigations. Lipids entered into the "omic" era, too, and there is a consolidated "lipidomics". The metabolic pathways of lipids that 25 years ago appeared to be complex are presently in a way that is much more complex and intriguing, being intimately connected with the intricate network of intracellular molecular traffic.

The impact of the new technologies for identifying genes, transfecting them into cells, and over expressing or silencing them was tremendous, in terms of innovation and growing knowledge. Of course, this also applies to the lipid field. However, serious perplexities were also generated, again regarding lipids, too. A similar situation applies to the exponential development of the use of transgenic animals: many findings were obtained that validated previous hypotheses. But unexpected results also emerged, which presumably reflect the present incomplete knowledge of the regulation mechanisms of gene expression. A further field that blossomed magnificently in recent decades is membrane lipidology, ranging from the release of fragments from membrane lipids, having a bioactive role, to the separation of some lipids and few proteins into more rigid domains (lipid rafts) holding peculiar properties, and the discovery of lipid anchors to protein. A completely novel notion is also the occurrence of bioregulators of sphingoid nature, deriving from membrane sphingolipids. Just to finish, surprising findings concern the role of lipids in a number of neural diseases and the relationship between diet lipids and brain function.

The "Neural Lipids" volume of the new Edition of the Handbook of Neurochemistry and Molecular Neurobiology was conceived to offer an update on present knowledge of neural lipids, evidencing the new advances and concepts but recalling the old basic ones in a perspective of continuity. Notwithstanding the efforts, the resulting view may probably be incomplete. However, it is surely sufficient to convince especially the newcomers to the field of the importance of structural and functional lipidology.

It is remarkable that some of the authors of the chapters collected in this Edition were authors of the previous edition, too: this is an unequivocal sign of continuity of interest and dedication to lipid science.

To finish on a sad note, two authors of this volume, Prof. L.A.Horrocks, and Prof. S.E.Pfeiffer, passed away before the publication of the volume. Prof. H.Moser, expert in peroxisomal physiopathology, also left us at the beginning of his engagement. Through the kind mediation of his wife, four of his co workers took care of continuing and terminating the work. Lloyd, Steve and Hugo continue to live in our memory and unchanged appreciation. This volume is dedicated to them.

Gianfrancesco Goracci
Guido Tettamanti

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Section 1

Biochemistry and Molecular Biology of Neural Lipids

1 Advances in Lipid Analysis/ Lipidomics – Analyses of Phospholipids by Recent Application of Mass Spectrometry

R. Taguchi

G. Tettamanti & G. Goracci (eds.), *Neural Lipids*, DOI 10.1007/978-0-387-30378-9 1,

Abstract: Mass spectrometry (MS) has become a most useful tool in the analysis of phospholipids. Analysis of molecular species of phospholipids adding to that of their classes and subclasses is necessary to elucidate their physiological functions. As analytical methods for lipidomics, basically three different types of approaches in the identification of phospholipid molecular species can be selected. The first one is shotgun LC-MS/MS analysis with data-dependent scan, the second one is structure-related focused methods such as precursor ion scanning or neutral loss scanning. Both types of data can be subjected to our search engine, "Lipid Search" (http://lipidsearch.jp), and most probable molecular species can be obtained with their compensated ion intensities. The lipid database for this search engine was constructed theoretically from their structure similarities and variations in polar head groups and fatty carbonyl chains. And identified individual molecular species can be automatically profiling according to their compensated ion intensities. The third method, such as multiple reaction monitoring, is also important for detecting very small amounts of targeted molecules such as lipid mediators or oxidized lipid metabolites. The choice of these three different kinds of methods seems to be very important for neurochemical research for detecting different kinds of lipid metabolites such as unknown lipid ligands, focused class of lipids, or targeted minor lipid mediators.

List of Abbreviations: CID, collision-induced dissociation; ESI, electrospray ionization; HPLC, high-performance liquid chromatography; LC, liquid chromatography; MS, mass spectrometry; PC, phos phatidylcholine; PE, phosphatidylethanolamine; PG, phosphatidylglycerol; PI, phosphatidylinositol; PS, phosphatidylserine; SM, sphingomyelin; UPLC, ultra performance liquid chromatography

1 Introduction

Lipids are a class of molecules thought to be very important, not only as energy source or constituents of biological membrane, but also as functional molecules concerning the many regulation steps in biological process (Di Paolo et al., 2004). Furthermore, recent research has revealed the roles of lipids, such as mediators of signal transduction and ligands receptors. And these functionally important lipid metabolites seem to be extremely rich in nerve system. Lipidomics is an important field in metabolomics, and is growing very rapidly by the recent advance in mass spectrometry (Han and Gross, 1994 and 2005; Pulfer and Murphy, 2003).

In lipidomics, techniques of mass spectrometry become very important. Furthermore, recent advances in mass spectrometry make it possible to get comprehensive analyses of lipid metabolites within the cells and tissues. Studies on lipidomics are essential to get further understanding of each physiological and biological function of proteins concerning lipid metabolism. In this process, studies on comprehensive profiling on lipid metabolites in the cells should be inevitable. In particular, to identify real lipid substrates for enzyme proteins, lipid ligands for receptor proteins, and lipid metabolites for its carrier proteins, lipidomics by mass spectrometry is very useful.

Another aim of lipidomics is to identify lipid molecules from mass spectrometry (MS) data and get profiling patterns of alteration of these molecules under specific circumstances. In these analytical processes of profiling, elucidation of unknown pathway or exact lipid substrate specificity of new enzyme proteins can be investigated.

Before the use of MS, phospholipids were mainly detected by identifying radioisotopes after thin layer chromatography, or by applying gas chromatography (GC) after derivatization (Yokoyama et al., 2000; Nor Aliza et al., 2001; Sana et al., 2002; Tserng and Griffin, 2003). But these methods can not be applied to identification of all molecules in a phospholipid mixture. By using classical ionization methods in mass spectrometry such as electron impact (EI) and chemical impact (CI), it has been very difficult to get molecular-related ions without any collapse. In these ionizations, fragment patterns of each molecule are basically used for criteria of identifications. Because of this reason, these methods were exclusively used for the mass measurement of purified single molecules. For the mixture, such as GC-MS were used after derivatization for effective separation and analytical sensitivities. But for the molecules difficult to be evaporated and ionized, useful methods such as GC-MS were not available. Thermospray ionization and atmospheric pressure chemical ionization (APCI) were also used in combination with high-performance