

Abel Lajtha

Editor

Guido Tettamanti

Gianfrancesco Goracci

Volume Editors

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Neural Lipids

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Handbook of Neurochemistry and Molecular Neurobiology

Neural Lipids

Abel Lajtha (Ed.)

Handbook of Neurochemistry and Molecular Neurobiology Neural Lipids

Volume Editors: Guido Tettamanti and Gianfrancesco Goracci

With 120 Figures and 56 Tables

Editor

Abel Lajtha
Director
Center for Neurochemistry
Nathan S. Kline Institute for Psychiatric Research
140 Old Orangeburg Road
Orangeburg
New York, 10962
USA

Volume Editors

Guido Tettamanti
Department of Medical Chemistry, Biochemistry and
Biotechnology
Via Saldini 50
20133, Milan
Italy

Gianfrancesco Goracci
Department of Internal Medicine
Section of Biochemistry
University of Perugia
via del Giochetto
06122 Perugia
Italy

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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 than 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

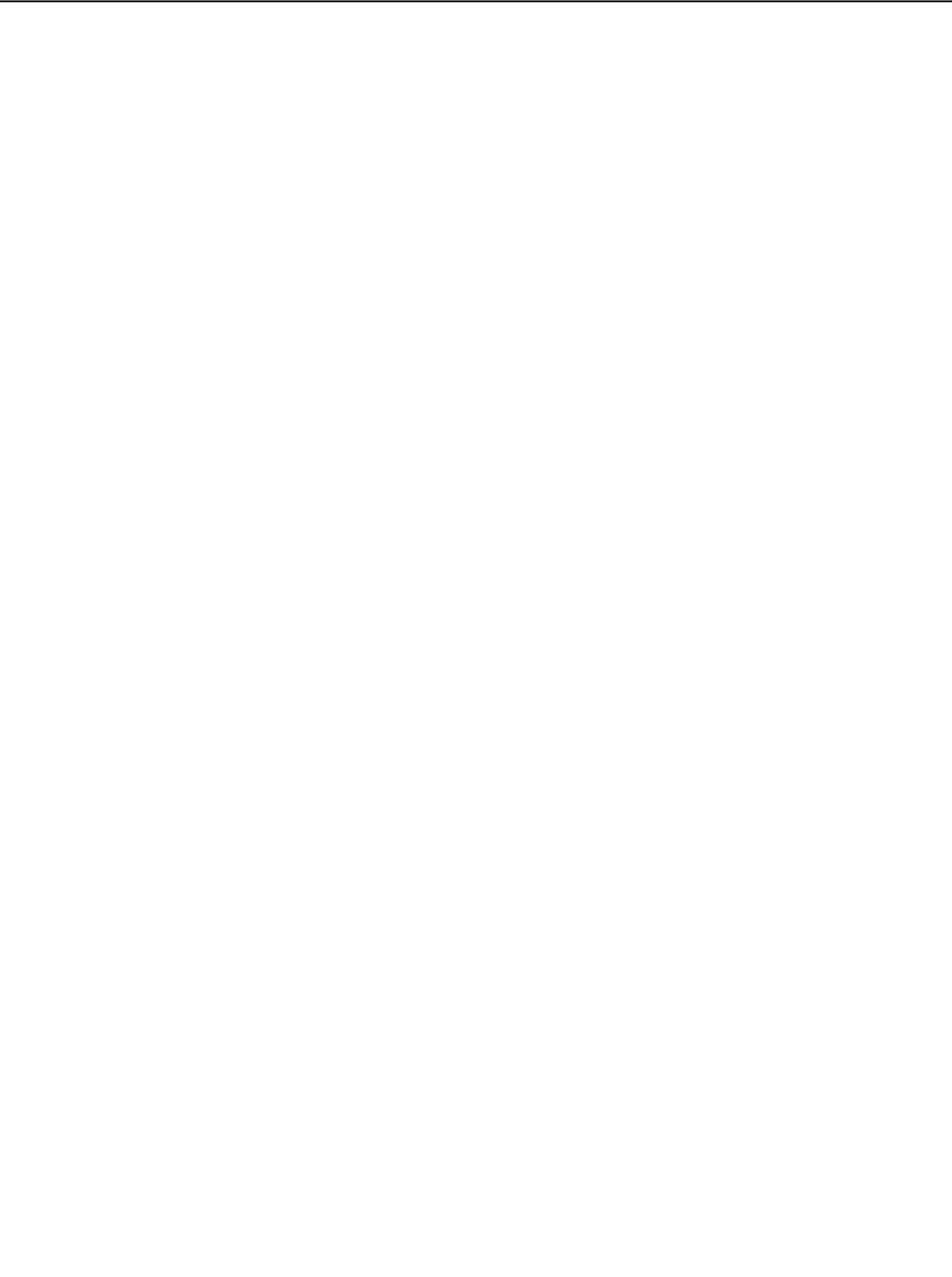


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Contributors

Hafiz Mohammad Abdul

Sanders Brown Center on Aging,
University of Kentucky, Lexington,
KY 40536, USA

Luigi Anastasia

Department of Medical Chemistry,
Biochemistry and Biotechnology Via Saldini 50,
20133, Milan, Italy

Maria Luisa Balestrieri

Department of Biochemistry and Biophysics,
Second University of Naples, Via L. De Crecchio 7,
80138 Naples, Italy

Rashmi Bansal

Department of Neuroscience, University of Connecticut
Medical School, 263 Farmington Avenue,
Farmington, CT 06030 3401, USA

Michela Barichella

Parkinson Institute,
Istituti Clinici di Perfezionamento,
Via Bignami, 1
20126 Milan, Italy
Email: barichella@parkinson.it

Jean Marie Bourre

INSERM, U 705, CNRS, UMR 7157,
200 rue du Faubourg Saint Denis,
75745 Paris cedex 10, France
Email: jean.marie.bourre@fwidal.inserm.fr

Annette Brand Yavin

IBCHN, London Metropolitan University,
166 220 Holloway Road,
London N7 8DB, UK

Anja U. Bräuer

Institute of Cell Biology & Neurobiology,
Center for Anatomy,
Charité Universitätsmedizin Berlin,
Phillipstrasse 12, 10115 Berlin, Germany

David N. Brindley

Signal Transduction Research Group,
Department of Biochemistry,
University of Alberta, Edmonton, Alberta,
T6G 2S2, Canada
Email: david.brindley@ualberta.ca

James R. Van Brocklyn

The Ohio State University Medical Center,
4164 Graves Hall,
333 W. 10th Ave.,
Columbus, OH 43210 , USA
Email: james.vanbrocklyn@osumc.edu

Alessandra Bulbarelli

Department of Experimental Medicine,
University of Milano Bicocca,
Via Cadore, 48,
20052 Monza (MI), Italy

Sandra Buratta

Department of Internal Medicine,
Biochemistry Section, University of Perugia, via del
Giochetto, 06122 Perugia, Italy

D. Allan Butterfield

Department of Chemistry, Center of Membrane
Sciences, and Sanders Brown Center on Aging,
University of Kentucky, Lexington KY 40506, USA
Email: dabcs@uky.edu

Antonella Di Campi

Department of Cell Biology and Oncology,
Consorzio Mario Negri Sud,
66030 Santa Maria Imbaro (Chieti), Italy

Mehmet Cansev

Department of Brain and Cognitive Sciences,
Massachusetts Institute of Technology,
Cambridge MA, 02139, USA
Department of Pharmacology and Clinical
Pharmacology, Uludag University Medical School,
Gorukle, Bursa, 16059, Turkey

Emanuela Cazzaniga

Department of Experimental Medicine,
University of Milano Bicocca,
Via Cadore, 48,
20052 Monza (MI), Italy
Email: emanuela.cazzaniga@unimib.it

Lanfranco Corazzi

Department of Internal Medicine,
Section of Biochemistry,
University of Perugia,
06122 Perugia, Italy
Email: corazzi@unipg.it

Giovanni D'Angelo

Department of Cell Biology and Oncology,
Consorzio Mario Negri Sud,
66030 Santa Maria Imbaro (Chieti), Italy

Akhlaq A. Farooqui

Department of Molecular and Cellular Biochemistry,
1645 Neil Avenue,
Columbus, Ohio 43210 1218, USA

Tahira Farooqui

Department of Molecular and Cellular Biochemistry and
Department of Entomology,
The Ohio State University, Columbus,
Ohio 43210, USA

Simon Ngamli Fewou

Department of Neuroscience,
University of Connecticut Health Center,
P.O. Box 3401, 263 Farmington Avenue,
Farmington, CT 06030 3401, USA
Email: nfsimon@uchc.edu, sfewou@yahoo.com

Paolo Gallo

Multiple Sclerosis Centre Veneto Region,
First Neurology Clinic Department of Neurosciences,
Via Giustiniani, 5 35128 Padova, Italy
Email: paolo.gallo@unipd.it

Gianfrancesco Goracci

Department of Internal Medicine,
Section of Biochemistry, University of Perugia,
via del Giochetto, 06122 Perugia, Italy
Email: goracci@unipg.it

Francesca Grassivaro

Multiple Sclerosis Centre Veneto Region,
First Neurology Clinic Department of Neurosciences,
Via Giustiniani, 5 35128 Padova, Italy

Hermann Josef Gröne

Department of Cellular and Molecular Pathology,
German Cancer Research Center,
Im Neuenheimer Feld 280,
69120 Heidelberg, Germany

Yusuf A. Hannun

Department of Biochemistry and Molecular Biology,
Medical University of South Carolina,
Charleston, South Carolina 29425, USA
Email: hannun@muscc.edu

Silvia Locatelli Hoops

Kekulé Institut für Organische Chemie und Biochemie
der Universität Bonn, Gerhard Domagk Str. 1,
53121 Bonn, Germany

Lloyd A. Horrocks

Department of Molecular and Cellular Biochemistry,
The Ohio State University, Columbus,
1645 Neil Avenue,
Columbus, Ohio 43210 1218, USA
Email: horrocks.2@osu.edu

Nicole Jackman

Department of Neuroscience, University of Connecticut
Medical School, 263 Farmington Avenue,
Farmington, CT 06030 3401, USA

Richard Jennemann

Department of Cellular and Molecular Pathology,
German Cancer Research Center,
Im Neuenheimer Feld 280,
69120 Heidelberg, Germany
Email: r.jennemann@dkfz.de

Thomas Kolter

Kekulé Institut für Organische Chemie und Biochemie
der Universität Bonn, Gerhard Domagk Str. 1,
53121 Bonn, Germany

Jacqueline M. Kraveka

Division of Hematology/Oncology, Department of
Pediatrics, Medical University of South Carolina,
Charleston, South Carolina 29425, USA

Robert Ledeen

New Jersey Medical School, UMDNJ,
Dept. Neurology & Neurosciences MSB H506,
185 South Orange Ave.,
Newark, NJ 07103, USA
Email: ledeenro@umdnj.edu

Lynette Lim

Department of Biological Sciences,
Centre for Life Sciences,
28 Medical Drive, #04 21,
Singapore 117607

Mauro Maccarrone

Department of Biomedical Sciences, University of
Teramo, Teramo, Italy
IRCCS C. Mondino, Mondino Tor Vergata Center for
Experimental Neurobiology, Rome, Italy
Email: mmaccarrone@unite.it

Vincenzo Di Marzo

Endocannabinoid Research Group at the Institute of
Biomolecular Chemistry, National Research Council,
Via Campi Flegrei 34, Comprensorio Olivetti, Bldg. 70,
80078 Pozzuoli (NA), Italy
Email: vdimarzo@icmib.na.cnr.it

Massimo Masserini

Department of Experimental Medicine,
University of Milano Bicocca,
Via Cadore, 48
20052 Monza (MI), Italy

Maria Antonietta De Matteis

Department of Cell Biology and Oncology,
Consorzio Mario Negri Sud,
66030 Santa Maria Imbaro (Chieti), Italy
Email: dematteis@negrisud.it

Andrea Mauri

Parkinson Institute, Istituti Clinici di Perfezionamento,
Via Bignami, 1,
20126 Milan, Italy

Gerrit van Meer

Membrane Enzymology Bijvoet Center / Institute of
Biomembranes, Utrecht University, Padualaan 8,
3584 CH Utrecht, The Netherlands

Rita Mozzi

Department of Internal Medicine,
Biochemistry Section, University of Perugia,
via del Giochetto, 06122 Perugia, Italy
Email: mozzi@unipg.it

Natalia N. Nalivaeva

Institute of Molecular and Cellular Biology,
Faculty of Biological Sciences,
University of Leeds, Leeds, LS2 9JT, UK
I.M. Sechenov Institute of Evolutionary Physiology and
Biochemistry, Russian Academy of Sciences,
44 Moris Thorez avenue, 194223 St. Petersburg, Russia
Email: n.n.nalivaeva@leeds.ac.uk

Vincenza Nardicchi

Department of Internal Medicine,
Section of Biochemistry, University of Perugia,
via del Giochetto, 06122 Perugia, Italy

Stefania Petrosino

Endocannabinoid Research Group at the Institute of
Biomolecular Chemistry, National Research Council,
Via Campi Flegrei 34, Comprensorio Olivetti,
Bldg. 70, 80078 Pozzuoli (NA), Italy

Gianni Pezzoli

Parkinson Institute, Istituti Clinici di Perfezionamento,
Via Bignami, 1,
20126 Milan, Italy

Steven E. Pfeiffer

Department of Neuroscience,
University of Connecticut Medical School,
263 Farmington Avenue, Farmington,
CT 06030 3401, USA

James Powers

Department of Pathology, University of Rochester
Medical Center, Rochester, NY, USA

Gerald V. Raymond

Department of Neurogenetics, Kennedy Krieger
Institute, 707 North Broadway, Baltimore,
MD 21205, USA
Email: raymond@kennedykrieger.org

Luciano Rinaldi

Multiple Sclerosis Centre Veneto Region,
First Neurology Clinic Department of Neurosciences,
Via Giustiniani, 5 35128 Padova, Italy

Rita Roberti

Department of Internal Medicine,
Section of Biochemistry,
University of Perugia,
06122 Perugia, Italy

Konrad Sandhoff

Kekulé Institut für Organische Chemie und Biochemie
der Universität Bonn, Gerhard Domagk Str. 1,
53121 Bonn, Germany

Roger Sandhoff

Department of Cellular and Molecular Pathology,
German Cancer Research Center,
Im Neuenheimer Feld 280,
69120 Heidelberg, Germany

Chiara Savardi

Parkinson Institute, Istituti Clinici di Perfezionamento,
Via Bignami, 1,
20126 Milan, Italy

Agnes Simonyi

Biochemistry Department,
M743, Medical Science Building,
University of Missouri,
Columbia, MO 65212, USA

Steven Steinberg

Department of Neurogenetics, Kennedy Krieger
Institute, 707 North Broadway, Baltimore,
MD 21205, USA

Birgit Stoffel Wagner

Department of Clinical Biochemistry,
University of Bonn, 53127 Bonn, Germany
Email: Birgit.Stoffel.Wagner@ukb.uni-bonn.de

Grace Y. Sun

Biochemistry Department,
M743, Medical Science Building,
University of Missouri,
Columbia, MO 65212, USA
Email: sung@missouri.edu

Albert Y. Sun

Department of Medical Pharmacology and Physiology,
University of Missouri, Columbia,
MO 65211, USA

Ryo Taguchi

Department of Metabolome,
Graduate School of Medicine, The University of Tokyo,
7-3-1 Hongo, Bunkyo-ku, Tokyo 113, Japan
Email: rytagu@m.u-tokyo.ac.jp

Guido Tettamanti

Department of Medical Chemistry, Biochemistry and
Biotechnology Via Saldini 50, 20133, Milan, Italy
IRCCS Policlinico San Donato, Via Morandi 30,
20097 San Donato Milanese, Milan, Italy
Email: guido.tettamanti@unimi.it

Anthony J. Turner

Institute of Molecular and Cellular Biology,
Faculty of Biological Sciences,
University of Leeds, Leeds, LS2 9JT, UK
Email: a.j.turner@leeds.ac.uk

Ismail H. Ulus

Department of Brain and Cognitive Sciences,
Massachusetts Institute of Technology,
Cambridge MA, 02139, USA
Department of Pharmacology and Clinical
Pharmacology, Uludag University Medical School,
Gorukle, Bursa, 16059, Turkey

Mariella Vicinanza

Department of Cell Biology and Oncology,
Consorzio Mario Negri Sud,
66030 Santa Maria Imbaro (Chieti), Italy

Paul Watkins

Department of Neurogenetics, Kennedy Krieger
Institute, 707 North Broadway, Baltimore,
MD 21205, USA

Markus R. Wenk

Department of Biological Sciences and Department of
Biochemistry,
Centre for Life Sciences,
28 Medical Drive, #04-21,
Singapore 117607
Email: bchmrw@nus.edu.sg

Herbert Wiegandt

Department of Cellular and Molecular Pathology,
German Cancer Research Center,
Im Neuenheimer Feld 280
69120 Heidelberg, Germany

Gusheng Wu

Department of Neurology and Neurosciences,
University of Medicine and Dentistry of New Jersey,
New Jersey Medical School, 185 So Orange Ave.,
Newark, NJ 07103, USA

Richard J. Wurtman

Department of Brain and Cognitive Sciences,
Massachusetts Institute of Technology,
Cambridge MA, 02139, USA
Email: dick@mit.edu

Ephraim Yavin

IBCHN, London Metropolitan University
166 220 Holloway Road,
London N7 8DB, UK
Email: ephraim.yavin@gmail.com



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

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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, phosphatidylcholine; 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