

Preface

Neurochemical importance of ether lipids is becoming increasingly evident. These lipids include plasmalogen and platelet activating factor. They play crucial roles in membrane fusion, ion transport, inflammation, oxidative stress, and learning and memory. Significant advances have been made in our understanding of structure and functions of plasmalogens and platelet activating factor in neural and non-neural tissues. Increased degradation of plasmalogens is associated with neurochemical and neuropathological changes associated with acute neural trauma (stroke, spinal cord trauma, and head injury) and neurodegenerative diseases (such as Alzheimer disease). The decrease in activity of plasmalogen-synthesizing enzymes is involved in peroxisomal disorders (such as Zellweger syndrome and Rhizomelic chondrodysplasia punctata). The increase in platelet activating factor levels has been reported to occur in ischemic injury, bacterial meningitis, AIDS, prion diseases, and multiple sclerosis. Miller-Dieker lissencephaly is caused by a mutation in PAF-acetyl hydrolase. In the past decade, there has been considerable development not only in our knowledge of the biochemistry of ether lipids but also in our understanding of signal transduction processes associated with their metabolism in the brain. The molecular mechanism that governs the transfer of the death signal from neural cell surface to the nucleus depends upon levels of lipid mediators generated by the degradation of ether lipids and crosstalk among ether lipid, diacyl glycerophospholipid, and glycosphingolipid-derived lipid mediators. This cross-talk modulates the intensity of oxidative stress and neuroinflammation. Thus, interactions among ether lipid, diacyl glycerophospholipid, and glycosphingolipid-derived lipid mediators play a major role in neuronal cell injury and death following acute neural trauma and neurodegenerative diseases. At present, it is unclear whether these processes are primary initiating points in neurodegeneration, or if they are the end result of the neurodegenerative process itself. In recent years, we have been empowered by technological advances in lipidomics, proteomics, and genomics. Investigators are using these techniques not only to identify and determine levels of lipid mediators but also for developing diagnostic test for neurodegenerative diseases associated with altered ether lipid metabolism.

The purpose of this monograph is to present the readers with a coherent overview and cutting edge information in a manner that is useful not only to students and

teachers but also to researchers and physicians. This monograph has 12 chapters. The first chapter describes the occurrence and importance of ether lipids in brain. Chapters 2 and 3 cover cutting-edge information on the biosynthesis and degradation of plasmalogens in the central nervous system. Chapter 4 describes the determination and purification of plasmalogen-selective phospholipase A_2 and lysoplasmalogenase from brain. Chapters 5 and 6 are devoted to roles and involvement of plasmalogens in neurological disorders. Chapters 7 and 8 describe the biosynthesis and degradation of platelet-activating factor in the central nervous system. Chapters 9 and 10 describe the functions and association of platelet activating factors with neurological disorders. Chapter 11 deals with neurochemical effects of antitumor ether lipids. Finally, Chapter 12 provides readers and researchers with perspective that will be important for future research work on bioactive ether lipids. Our writing style and demonstrated ability to present complicated material on bioactive ether lipid metabolism makes this book particularly accessible to neuroscience graduate students, teachers, and fellow researchers. It can be used as a supplement for a range of neuroscience courses. This monograph is essential reading for the busy physician or pathologist who wants to be up to date with the latest developments on plasmalogens and platelet-activating factor metabolism.

Clinicians will find this book useful for understanding the molecular aspects of neurodegeneration in stroke and Alzheimer disease that are mediated by plasmalogen-selective phospholipase A_2 and PAF acetyl hydrolase. To our knowledge, no one has written a monograph on bioactive ether lipids and so this monograph is the first to provide students, teachers, researchers, and clinicians a comprehensive description of metabolism and role of plasmalogen and platelet-activating factor along with abnormal signal transduction processes in neurological disorders.

The choices of topics presented in this monograph are personal. They are not only based on our interest in ether lipid metabolism in neurological disorders, but also in an area where major progress has been made. We have tried to ensure uniformity in mode of presentation as well as a logical progression from one topic to another, and have provided extensive referencing. For the sake of simplicity and uniformity, a large number of figures and line diagrams of signal transduction pathways are also included. We hope that our attempt to integrate and consolidate the knowledge of signal transduction processes associated with ether lipid metabolism in brain will provide the basis of more dramatic advances and developments on the involvement of bioactive ether lipids in neurological disorders.

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Metabolism and Functions of Bioactive Ether Lipids in
the Brain

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2008, XX, 260 p., Hardcover

ISBN: 978-0-387-77400-8