PREFACE

Alzheimer's disease (AD) is the most common cause of dementia. The term "dementia" is derived from the Latin word *demens*, meaning "being out of one's mind," and has been used since the 13th century. AD has been recognized as a distinct entity since the publication of Alzheimer's description of a patient with presenile dementia in 1906. The first biochemical identification of amyloid beta (Aβ) as the major component of amyloid plaques, a key neuropathological lesion in AD, was published in 1984 with the seminal work of Dr. George Glenner. The latter discovery led to the amyloid cascade hypothesis of AD, with a focus on developing amyloid directed therapeutic approaches. The latter have all failed in clinical trials thus far. More recently, there is growing body of genetic, transcriptomic, and proteomic data pointing to the complexity of AD pathogenesis. This has resulted in a greater diversity of therapeutic approaches being attempted—in effect, resulting in "more shots on goal," with the prospect that at least some of these approaches will be efficacious. Hence, despite the many failures of AD therapeutic clinical trials, this is a hopeful time in AD research. There is a growing anticipation that our greater understanding of the underlying multifactorial pathogenesis of AD will result in effective therapeutic interventions in the near future.

In this book, we present reviews with the most current information on several critical aspects of AD, providing the readers with a broad picture of the underlying neuropathology, genetics, proteomics, risk factors, novel biomarkers, and potential interventions. Chapters 1–5 discuss the underlying AD pathogenesis using genomic and proteomic approaches, linking diverse pathways that can lead to complex metabolic dysfunction. Chapter 6 reviews the potential role of trace metals in AD, while Chapter 7 examines the diversity of Aβ species involved in AD pathology. Chapter 8 discusses the contributions of white matter degeneration in AD. Chapter 9 examines the potential intriguing role of the brain-gut-microbiota axis in mediating AD. Chapters 10 and 11 discuss potential biomarkers for AD, such as deficits in ocular exploration and early language impairments, respectively. Chapters 12–15 examine possible novel preventative and/or therapeutic methodologies such as exercise, optimizing depression therapy, and diverse psychosocial interventions.

We would like to thank all the authors for their diligent work in contributing toward this book. The 15 chapters review diverse facets of AD, which together paint a comprehensive picture of the pathogenesis, associated risk factors, novel biomarkers, and potential therapeutic targets. We believe that this book will encourage readers to delve deeper into this field and take up the critical challenge of working toward effective treatments for AD and related dementias.

Thomas Wisniewski, MD
Gerald J. and Dorothy R. Friedman Professor
at the New York University Alzheimer's Disease Center
Professor of Neurology, Pathology and Psychiatry
New York University School of Medicine
New York, USA