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The Biology of Alzheimer Disease

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The Biology of Alzheimer Disease

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Front cover artwork: Four self-portraits by the artist William Utermohlen, an American who lived in London, chronicle his experience with Alzheimer disease. Utermohlen was diagnosed at the age of 60; his powerful, emotionally complex depictions of the disease have garnered wide acclaim. The first in this series (*top left*) was painted in 1995, when he was diagnosed with the disease. The artist's wife, an art critic, has speculated that a growing awareness of cognitive decline may have contributed to the artist's depiction of himself behind windowpanes that resemble prison bars. The other pictures, which Utermohlen created over the course of the next 5 years, show a progressive loss of the ability to depict complex spatial relationships and provide evidence of growing perceptual difficulties. Soon after completing the last sketch, he ceased to work. (William Utermohlen's work reprinted with kind permission from Patricia Utermohlen and the Galerie Beckel Odille Boïcos, Paris.)

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Preface

ATTEMPTING TO ORGANIZE AND REVIEW THE EXTENSIVE BODY of scientific literature on the biological basis of Alzheimer disease (AD) would seem to be a daunting task. The idea of preparing a book that does so comprehensively emerged from many discussions over the last decade about how this field of inquiry was progressing and how one might integrate the diversity of approaches and findings that it has generated. The editors of this volume took on the responsibility of identifying and sequencing the major topics to be covered and assembling a group of expert authors. As such, we are well aware that there are various ways such a huge body of research could be covered and that some topics will perforce receive more or less attention than others. The editors chose highly knowledgeable and scientifically active investigators in Alzheimer biology to contribute chapters on topics in which they have deep expertise. We are most grateful that virtually everyone invited to write for the book quickly agreed to participate, despite having very busy schedules. The diverse scientific viewpoints and collective wisdom of this talented group will, we hope, enable the volume to provide value to the broad biomedical community as it strives to achieve the intellectually fascinating and medically critical goal of solving AD.

The editors apologize in advance to those readers who may find missing elements or points of disagreement or overlap among the array of scientific findings reviewed here, and we recognize that no one volume can do full justice to this intense and rapidly advancing field. However, we would point out that, depending on its reception, this first comprehensive book reviewing the biological underpinnings of AD will be revised, updated, and thus improved within a few years. In this sense, we hope to have the opportunity to respond to issues we overlooked or covered insufficiently, given the space and time available to complete a project of this magnitude. It is likely that revised editions of this book—if they come to pass—will be even more detailed and compelling than this first effort. Nevertheless, we are hopeful that the multifaceted subjects covered here in considerable depth by distinguished authorities will prove useful to a broad audience of undergraduate, graduate, and medical students, postdoctoral fellows, junior and senior investigators, and, importantly, scientists and clinicians working outside the field of AD research.

Readers familiar with the Alzheimer field may notice that some chapters are coauthored by investigators who have had differing views of the topic under review or have sometimes been competitors. The editors purposely chose this path to encourage the synthesis of diverse perspectives and attempt to achieve clarity and common ground on unsettled issues. We are grateful to all of our chapter authors but particularly to those who at first pass found themselves facing the challenging task of melding disparate ideas and data.

We encourage readers not only to peruse chapters on topics that particularly intrigue—or confuse—they but also to read the first and last chapters of the book. Here, the editors have tried to step back from the wealth of details and convey a sense of what has motivated the global quest to understand the biology of AD, how sometimes competing concepts and lines of inquiry have proceeded, and, most importantly, where we believe this scientifically rich and therapeutically promising field is headed.

The editors thank Barbara Acosta, Richard Sever, and their colleagues at Cold Spring Harbor Laboratory Press for their excellent editorial and compositional efforts in putting this book together and their patience with the inevitable delays and minor crises that arise during such an ambitious undertaking. Each of the editors owes a very special thanks to past and current members of his

Preface

respective laboratory and other local colleagues for innumerable discussions about the science of AD and how to think about its many unresolved questions. We also thank our gifted and dedicated administrative assistants who helped us in this work, especially Ms. Nicole Boucher (at BWH/HMS). One of us (D.J.S.) had the benefit of the careful bibliographical research, data analysis, and sage editorial advice of Marcia Podlisny, Ph.D., who had helped organize information relevant to this volume during an earlier effort some years ago. Finally, we are indebted to our families for their support and forbearance as we added the creation of this book to our already numerous responsibilities. We hope that the outcome will justify the collective efforts of the authors and editors and help illuminate the path toward scientifically well-grounded therapeutics that could ultimately prevent this common and devastating disorder.

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