

Preface

The field of neurodegenerative diseases is undergoing an unprecedented revolution. The past decade has seen the identification of new mutation mechanisms, such as triplet repeat expansions, and new genes causing familial forms of common neurodegenerative diseases, such as Parkinson's and Alzheimer's diseases. Cellular and animal models based on this genetic information are now available and, importantly, common mechanisms are rapidly emerging among diseases that were once considered unrelated. The field is poised for the development of new therapies based on high throughput screenings and a better understanding of the molecular and cellular mechanisms leading to neurodegeneration.

Molecular Mechanisms of Neurodegenerative Diseases reviews recent progress in this exploding field. By nature, such a book cannot be all inclusive. It focuses on Alzheimer's, Parkinson's, and CAG triplet repeat diseases. In the first chapter, Bill Klein reviews the role of A β toxicity in the pathophysiology of Alzheimer's disease. This controversial issue is further examined in the context of transgenic models of Alzheimer's disease by LaFerla and colleagues. Sue Griffin and Robert Mruk, and Caleb Finch and collaborators, then examine the role of glial cells and inflammation in Alzheimer's disease; a review of the role of proteolysis in the generation of abnormal protein fragments by Hook and Mende-Mueller follows. Therapeutic opportunities offered by a better understanding of Alzheimer's disease pathophysiology are examined by Perry Molinoff and his colleagues at Bristol-Myers Squibb.

The chapter on proteolysis by Hook and Mende-Mueller identifies one of the recurring themes that is appearing among neurodegenerative diseases: the formation of abnormal protein fragments, whose misfolding may lead to a cascade of cellular defects, ultimately leading to cell death. Similarities between pathological processes in Parkinson's, Alzheimer's, and related diseases is also the theme of the chapter by Virginia Lee, John Trojanowski, and collaborators, which discusses the role of Tau and synuclein. Despite the identification of mutations in synuclein, and the presence of synuclein in Lewy bodies, the pathophysiology of Parkinson's disease, however, remains poorly understood. Joel Perlmuter and his colleagues review the information we have recently gained on the progression of the disease from brain imaging studies.

BethAnn McLaughlin and Russell Swerdlow then examine the role of dopamine and of mitochondrial dysfunction, respectively, in neurodegeneration.

The last chapters of the book deal with different and complementary aspects of CAG repeat diseases, including SCA1 (Orr and Zoghbi), SCA3 (Opal and Paulson), SBMA (Merry), and Huntington's disease. Chesselet and Levine compare the different mouse models of Huntington's disease, MacDonald and colleagues review the role of proteins interacting with huntingtin, and George Jackson discusses the potential of fly genetics to identify the molecular mechanisms of neurodegenerative diseases.

Despite their differences in focus, many chapters of *Molecular Mechanisms of Neurodegenerative Diseases* overlap, presenting the variety of viewpoints that pervade this dynamic field. Evidently, since new data appear every day, the chapters in a book can only provide the basis for understanding ongoing research. It is hoped that the ideas and concepts presented here will lead, within a few short years, to therapies that prevent, delay the onset, slow the progression, or even cure these devastating neurodegenerative illnesses.

Marie-Françoise Chesselet, MD, PhD

Molecular Mechanisms of Neurodegenerative Diseases

Chesselet, M.-F. (Ed.)

2001, XIII, 410 p., Hardcover

ISBN: 978-0-89603-804-2

A product of Humana Press