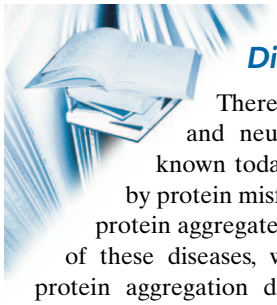


Protein Misfolding Diseases

There are more than 25 cell- and neurodegenerative diseases known today that are characterized by protein misfolding and deposition of protein aggregates in tissue. A major class of these diseases, which are often termed protein aggregation diseases and are mostly incurable, are the amyloid diseases. These include Alzheimer's disease (AD), type 2 diabetes (T2D), and the transmissible spongiform encephalopathies (TSEs). Despite their different etiologies, pathologies, and diverse disease-specific factors, and the fact that each of these diseases is characterized by tissue deposition of a different protein, it appears that they might have in common certain basic molecular mechanisms. In this context, extensive research has been performed within the past 20 years and has generated important, and in part also highly debated, pieces of knowledge, while a number of questions still remain to be answered. Uncovering the principles of protein misfolding, aggregation, and associated cell degeneration at the molecular and cellular levels is thus still a great challenge in (bio)chemical and biomedical research. Progress in that direction will assist in both elucidating the molecular basis of disease pathogenesis and developing novel therapeutic and diagnostic strategies.

The book *Protein Misfolding Diseases: Current and Emerging Principles and Therapies* is the impressive result of a joint editorial effort by Marina Ramirez-Alvarado, Jeffery W. Kelly, and Christopher M. Dobson, all three of whom are key contributors in this field, and contains articles written by a number of experts including both basic research scientists and clinicians. This book offers a broad, up-to-date, and comprehensive overview of the current knowledge about the molecular and cellular mechanisms of protein misfolding, related cell degeneration, and disease pathogenesis. In addition, it reviews a number of medical issues related to such diseases, focusing on currently used and emerging diagnostic and therapeutic strategies.

The book is very well organized and clearly written, and contains a large number of nice figures and illustrations, some in color, which certainly help to simplify the complex thematic material and to make it attractive to the reader. The contributions provide a sufficient body of background information, are concisely written, and contain many references, which makes them valuable bibliographic sources.

The book is divided into five main chapters. The first chapter reviews knowledge about the basic molecular and cellular mechanisms of protein misfolding, aggregation, and toxicity, and about quality control, as derived both from in vitro studies and from in vivo studies of model systems of disease, including worm, fly, and mouse models.

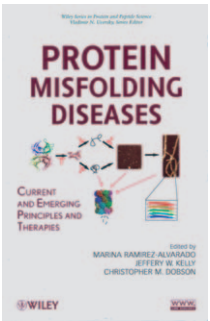
The second chapter offers a thorough insight into the molecular mechanisms of some of the most extensively studied diseases. These include those that affect the central nervous system, such as AD, Huntington's disease (HD), TSEs, and amyotrophic lateral sclerosis (ALS), and also other protein misfolding diseases such as systemic or dialysis-related amyloidosis, T2D, cystic fibrosis, and Gaucher disease. Importantly, most of the contributions in this chapter not only provide detailed mechanistic insights but also discuss therapeutic concepts.

The third chapter first focuses on the role of accessory molecules in protein misfolding and aggregation, such as metals, extracellular matrix components, and the plasma glycoprotein serum amyloid P component (SAP), which appears to be present in all amyloid deposits studied in vivo. In addition to the mechanistic overview, insights into disease modifying approaches based on the above molecules and mechanisms are also included. A second focus of this chapter is on the role of certain inherently unavoidable in vivo biochemical processes, such as oxidative stress and aging, in causing protein misfolding and disease pathogenesis. Oxidative stress is manifested, for example, in lipid peroxidation and related oxidative damage of proteins, while aging and probably the age-associated decline in native cellular protective mechanisms are major risk factors for the development of a number of neurodegenerative diseases such as AD, Parkinson's disease (PD), and HD.

The fourth chapter offers a comprehensive and thorough overview of the current state of development of diagnostic methods, such as amyloid imaging, biomarker identification, and clinical evaluation, and of the currently used therapeutic intervention strategies in various misfolding diseases, including AD, HD, and several other amyloid diseases.

The final chapter provides an excellent overview of emerging and exciting concepts for the development of therapeutic methods and novel treatment or prophylactic strategies for protein misfolding diseases. These approaches include, for example, strategies that use antibodies, vaccines, small organic molecules, modified peptides, small molecules as "kinetic stabilizers", and strategies to control gene expression of molecular chaperones or amyloidogenic proteins.

In summary, this book succeeds perfectly in combining detailed mechanistic depth and results from top-class research, which are required to attract the more specialized readers, with the thematic broadness and timely coverage of the



Protein Misfolding Diseases Current and Emerging Principles and Therapies. Wiley Series in Protein and Peptide Science. Edited by Marina Ramirez-Alvarado, Jeffery W. Kelly, and Christopher M. Dobson. John Wiley & Sons, Hoboken 2010. 1046 pp., hardcover € 169.00.—ISBN 978-0471799283

field of protein misfolding diseases that makes it also highly appealing to non-specialist readers. It is a fascinating, very enjoyable, and valuable read for scientists of a wide spectrum of disciplines including (bio)chemistry, biology, biophysics, and medicine, since it provides in-depth reviews of knowledge gained from interdisciplinary research on many aspects of both basic and applied science in this highly topical field.

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DOI: 10.1002/anie.201007008

