# protein misfolding in neurodegenerative diseases mechanisms and therapeutic strategies enzyme inhibitors series

**#protein misfolding #neurodegenerative diseases #enzyme inhibitors #disease mechanisms #therapeutic strategies**

Explore the critical role of protein misfolding in the pathogenesis of neurodegenerative diseases, examining underlying disease mechanisms. This resource also delves into promising therapeutic strategies, particularly focusing on the development and application of enzyme inhibitors as a potential avenue for treatment.



## Protein Misfolding in Neurodegenerative Diseases

Research focused on protein folding, misfolding, and aggregation is leading to major advances across biochemistry and medicine. The elucidation of a folding code is proving to be of extreme importance in the postgenomic era, where a number of orphan genes have been identified for which no clear function has yet been established. This research is starting to shed light on the molecular and biochemical basis of a number of neurodegenerative diseases of dramatic impact. Protein Misfolding in Neurodegenerative Diseases: Mechanisms and Therapeutic Strategies addresses key issues concerning protein misfolding and aggregation in neurodegenerative diseases. Building on recent developments, including the recognition of protein misfolding as both a marker and a causal agent, the text presents the work of those who are actively pursuing more effective treatments, as well as preventative measures, and a possible cure. These include the use of molecular chaperones to control misfolding and novel pharmaceuticals, as well as the potential role of various inhibitors and NSAIDS. A Comprehensive Multifaceted Examination of the Complex Causal Agents Implicated in Protein Misfolding Divided into five sections, this groundbreaking text provides up-to-date accounts for Alzheimer’s, Parkinson’s, Huntington’s, Amyotrophic Lateral Sclerosis and Transmissible Spongiform Encephalitis. It also explores the highly likelihood that multiple factors, including oxidative stress, play a role in these complex diseases.

## Metal-Based Neurodegeneration

Neurodegenerative diseases of the human brain appear in variousforms, resulting in disorders of movement and coordination,cognitive deterioration and psychiatric disturbances. Many of thekey factors

leading to neurodegenerative diseases are similar,including the dysfunction of metal ion homeostasis, redox-activemetal ions generating oxidative stress, and intracellular inclusionbodies. Metal-based Neurodegeneration presents a detailed surveyof the molecular origins of neurodegenerative diseases. Eachchapter is dedicated to a specific disease, presenting the latestscientific findings, including details of their biochemicalactors (proteins or peptides), their normal and pathologicalconformations, and a description of the diseases characteristics,with an emphasis on the role of metal-induced oxidative stress,which can result in the production of intracellular aggregates oftarget proteins and peptides. Topics covered include: Brain function, physiology and the blood-brain barrier Immune system and neuroinflammation Aging and mild cognitive impairment, MCI Parkinson's Disease Alzheimer's Disease Creutzfelt-Jakob and related prion diseases Alcoholic Brain Damage Therapeutic strategies to combat the onset and progression ofneurological diseases This extensively updated, full colour, second edition ofMetal-based Neurodegeneration is an essential text forresearch scientists and clinicians working in gerontology,neuropathology, neurochemistry, and metalloprotein mechanisms.

## Leucine-Rich Repeat Kinase 2 (LRRK2)

This is the first book to assemble the leading researchers in the field of LRRK2 biology and neurology and provide a snapshot of the current state of knowledge, encompassing all major aspects of its function and dysfunction. The contributors are experts in cell biology and physiology, neurobiology, and medicinal chemistry, bringing a multidisciplinary perspective on the gene and its role in disease. The book covers the identification of LRRK2 as a major contributor to the pathogenesis of Parkinson's Disease. It also discusses the current state of the field after a decade of research, putative normal physiological roles of LRRK2, and the various pathways that have been identified in the search for the mechanism(s) of its induction of neurodegeneration.

## Molecular Chaperones in Health and Disease

Molecular chaperones are involved in a wide variety of essential cellular processes in living cells. A subset of molecular chaperones have been initially described as heat shock proteins protecting cells from stress damage by keeping cellular proteins in a folding competent state and preventing them from irreversible aggregation. Later it became obvious that molecular chaperones are also expressed constitutively in the cell and are involved in complex processes such as protein synthesis, intracellular protein transport, post-translational modification and secretion of proteins as well as receptor signalling. Hence, it is not surprising that molecular chaperones are implicated in the pathogenesis of many relevant diseases and could be regarded as potential pharmacological targets. Starting with the analysis of the mode of action of chaperones at the molecular, cellular and organismic level, this book will then describe specific aspects where modulation of chaperone action could be of pharmacological and therapeutic interest.

## Neurodegenerative Diseases

This book highlights the pathophysiological complexities of the mechanisms and factors that are likely to be involved in a range of neuroinflammatory and neurodegenerative diseases including Alzheimer's disease, other Dementia, Parkinson Diseases and Multiple Sclerosis. The spectrum of diverse factors involved in neurodegeneration, such as protein aggregation, oxidative stress, caspases and secretase, regulators, cholesterol, zinc, microglia, astrocytes, oligodendrocytes, etc, have been discussed in the context of disease progression. In addition, novel approaches to therapeutic interventions have also been presented. It is hoped that students, scientists and clinicians shall find this very informative book immensely useful and thought-provoking.

## Oxidative Stress and Redox Signalling in Parkinson's Disease

Parkinson's Disease is the second most common neurodegenerative disorder affecting millions of people worldwide. In order to find neuroprotective strategies, a clear understanding of the mechanisms involved in the dopaminergic death of cells that progresses the disease is needed. Oxidative stress can be defined as an imbalance between the production of reactive species and the ability to detoxify them and their intermediates or by-products. Oxidative damage to lipids, proteins, and DNA has been detected in autopsies from individuals with Parkinson's Disease and so links can be made between oxidative stress and Parkinson's Disease pathogenesis. This book provides a thorough review of the mechanisms by which oxidative stress and redox signalling mediate Parkinson's Disease. Opening chapters bring readers up to speed on basic knowledge regarding oxidative stress and redox

signalling, Parkinson’s Disease, and neurodegeneration before the latest advances in this field are explored in detail. Topics covered in the following chapters include the role of mitochondria, dopamine metabolism, metal homeostasis, inflammation, DNA-damage and thiol-signalling. The role of genetics and gene-environment interactions are also explored before final chapters discuss the identification of potential biomarkers for diagnosis and disease progression and the future of redox/antioxidant based therapeutics. Written by recognized experts in the field, this book will be a valuable source of information for postgraduate students and academics, clinicians, toxicologists and risk assessment groups. Importantly, it presents the current research that might later lead to redox or antioxidant – based therapeutics for Parkinson’s disease.

## Protein Misfolding Diseases

An increasingly aging population will add to the number of individuals suffering from amyloid. Protein Misfolding Diseases provides a systematic overview of the current and emerging therapies for these types of protein misfolding diseases, including Alzheimer's, Parkinson's, and Mad Cow. The book emphasizes therapeutics in an amyloid disease context to help students, faculty, scientific researchers, and doctors working with protein misfolding diseases bridge the gap between basic science and pharmaceutical applications to protein misfolding disease.

## Tau oligomers

Neurofibrillary tangles (NFTs) composed of intracellular aggregates of tau protein are a key neuropathological feature of Alzheimer’s Disease (AD) and other neurodegenerative diseases, collectively termed tauopathies. The abundance of NFTs has been reported to correlate positively with the severity of cognitive impairment in AD. However, accumulating evidences derived from studies of experimental models have identified that NFTs themselves may not be neurotoxic. Now, many of tau researchers are seeking a “toxic” form of tau protein. Moreover, it was suggested that a “toxic” tau was capable to seed aggregation of native tau protein and to propagate in a prion-like manner. However, the exact neurotoxic tau species remain unclear. Because mature tangles seem to be non-toxic component, “tau oligomers” as the candidate of “toxic” tau have been investigated for more than one decade. In this topic, we will discuss our consensus of “tau oligomers” because the term of “tau oligomers” [e.g. dimer (disulfide bond-dependent or independent), multimer (more than dimer), granular (definition by EM or AFM) and maybe small filamentous aggregates] has been used by each researchers definition. From a biochemical point of view, tau protein has several unique characteristics such as natively unfolded conformation, thermo-stability, acid-stability, and capability of post-translational modifications. Although tau protein research has been continued for a long time, we are still missing the mechanisms of NFT formation. It is unclear how the conversion is occurred from natively unfolded protein to abnormally mis-folded protein. It remains unknown how tau protein can be formed filaments [e.g. paired helical filament (PHF), straight filament and twisted filament] in cells albeit in vitro studies confirmed tau self-assembly by several inducing factors. Researchers are still debating whether tau oligomerization is primary event rather than tau phosphorylation in the tau pathogenesis. Inhibition of either tau phosphorylation or aggregation has been investigated for the prevention of tauopathies, however, it will make an irrelevant result if we don’t know an exact target of neurotoxicity. It is a time to have a consensus of definition, terminology and methodology for the identification of “tau oligomers”.

## Molecular Mechanisms of Neurodegenerative Diseases

With the unprecedented identification of new mutation mechanisms in neurodegenerative diseases and the emergence of common mechanisms among diseases that were once considered unrelated, neurobiologists are 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. In Molecular Mechanisms of Neurodegenerative Diseases, Marie-Francoise Chesselet, MD, PhD, and a panel of leading researchers and neurologists from industry and academia critically review the most recent advances from different yet complementary points of view. Focusing on Alzheimer's, Parkinson's, and CAG triplet repeat diseases, the authors show how studies of cellular and genetically engineered animal models have enhanced our understanding of the molecular mechanisms of neurodegenerative diseases and may lead to the development of new therapeutics. Topics include the role of Ab toxicity, glial cells, and inflammation in Alzheimer's disease; the formation of abnormal protein fragments across several diseases, the impact of dopamine and mitochondrial dysfunction on neurodegeneration; and the potential of genetics to identify the molecular mechanisms of neurodegenerative diseases. Author-

itative and insightful, Molecular Mechanisms of Neurodegenerative Diseases synthesizes the novel ideas and concepts now emerging to create a fresh understanding of neurodegenerative disorders, one that promises to lead to powerful new therapies that prevent, delay the onset, slow the progression, or even cure these cruel diseases.

## The Role of AAA+ Proteins in Protein Repair and Degradation

ATPases Associated with diverse cellular Activities (AAA+) comprise a superfamily of proteins that are defined by the presence of the AAA+ domain containing canonical Walker A and B motifs required for ATP binding and hydrolysis. Members of this superfamily act on other proteins, DNA, RNA, or multicomponent complexes to affect their conformation or their assembly. There have been substantial advances in understanding the structure and mechanism of function of a large number of AAA+ proteins. In this Research Topic, review articles and original research papers discuss new aspects as well as provide a detailed overview of several AAA+ proteins, namely: ClpXP, Lon, ClpB, Hsp104, p97, AAA+ proteins of the proteasome, Rubisco activases, Torsin, Pontin, and Reptin.

## Design of Caspase Inhibitors as Potential Clinical Agents

Presents the Therapeutic Potential for Caspase Inhibitors: Present and Future Caspases represent one of the most specific protease families described to date. These extremely important enzymes are crucial to the destruction of aberrant cells – the body’s self-protection mechanism for warding off the growth of abnormal cells, many of which can promote cancer. Design of Caspase Inhibitors as Potential Clinical Agents introduces cutting-edge evidence regarding caspases’ role in pro-inflammatory responses. New research now shows that the inhibition of caspase function is a critical component for the treatment of many diseases, including: Arthritic and neurological disorders Lung disease Hereditary fever syndromes Inflammatory bowel and skin diseases Sepsis Liver fibrosis Outlines Efforts to Develop Molecule Inhibitors for Caspase Activity Transformation Under the editorial guidance of authoritative inflammatory disease, small molecule discovery, and apoptosis researchers, the book organizes the wide array of caspase literature into one convenient resource. It also summarizes the relative difficulty of transitioning a caspase small molecule inhibitor from the lab to the clinic and suggests approaches to circumvent this difficulty. Taking a novel, yet core approach to disease treatment, this seminal work sets the stage to combat a slew of debilitating diseases through groundbreaking drug development.

## Neurodegeneration

Neurodegeneration: Exploring Commonalities Across Diseases is the summary of a workshop hosted by the Institute of Medicine\\'s (IOM\\'s) Forum on Neuroscience and Nervous System Disorders in Spring 2012 to explore commonalities across neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), and frontotemporal dementia (FTD). Participants from academia; pharmaceutical and biotechnology industries; government agencies such as the National Institutes of Health and the U.S. Department of Veterans Affairs (VA); patient advocacy groups; and private foundations presented and identified potential opportunities for collaboration across the respective research and development communities. This report identifies and discusses commonalities related to genetic and cellular mechanisms, identifies areas of fundamental science needed to facilitate therapeutics development, and explores areas of potential collaboration among the respective research communities. Neurodegenerative diseases, such as Alzheimer\\'s disease, Parkinson\\'s disease, ALS, and FTD, are becoming increasingly prevalent in the United States due to an aging population. Implications are grave for quality of life and health care costs. Research on neurodegenerative diseases has expanded greatly over the past four decades. Nevertheless, fundamental questions remain about the biology of these diseases, and further insights into the mechanisms of these diseases would help to inform the development of effective means to prevent and to efficiently treat them. Recent findings have revealed certain commonalities in genetic and cellular mechanisms across neurodegenerative diseases. These findings suggest that it might be valuable - at least in some cases - to change the traditional way of studying these diseases by no longer seeing each as an independent entity, but rather as clinical variants of common cellular and molecular biological defects. This approach could help enhance basic scientific understanding of neurodegenerative disease, and could help with the development of biomarkers and new therapeutics.

## Neurodegenerative Diseases

Neurodegenerative diseases represent a very large group of heterogeneous disorders affecting specific subtypes of neurons in the brain. This book contributes insight both to the awareness of the brain and its neurodegenerative states. The chapters present current knowledge regarding genetics, molecular mechanisms, and new therapeutic strategies against neurodegenerative disorders. The book is intended to serve as a source to aid clinicians and researchers in the field, and also life science readers to increase their understanding and awareness of the clinical correlations, genetic aspects, neuropathological findings, and current therapeutic interventions in neurodegenerative diseases. I believe that this book will enlighten the curiosity for neurodegeneration and also encourage researchers to work on potentially effective molecular therapies for still mysterious neurodegenerative disorders.

## The Benefits of Natural Products for Neurodegenerative Diseases

Focuses on the effects of natural products and their active components on brain function and neurodegenerative disease prevention. Phytochemicals such as alkaloids, terpenes, flavanoids, isoflavones, saponins etc are known to possess protective activity against many neurological diseases. The molecular mechanisms behind the curative effects rely mainly on the action of phytonutrients on distinct signaling pathways associated with protein folding and neuro-inflammation. The diverse array of bioactive nutrients present in these natural products plays a pivotal role in prevention and cure of various neurodegenerative diseases, disorders, or insults, such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, traumatic brain injury, and other neuronal dysfunctions. However, the use of these antioxidants in the management of neurodegenerative conditions has so far been not well understood. This is a comprehensive collection addressing the effects on the brain of natural products and edible items such as reservatrol, curcumin, gingerol, fruits, vegetables, nuts, and marine products.

## The Prion Protein

A conformational transition of the cellular prion protein (PrPC) into an aberrantly folded isoform designated scrapie prion protein (PrPSc) is the hallmark of a variety of neurodegenerative disorders collectively called prion diseases. They include Creutzfeldt-Jakob disease and Gerstmann-Stäussler-Scheinker syndrome in humans, scrapie in sheep, bovine spongiform encephalopathy (BSE) in cattle and chronic wasting disease (CWD) in free-ranging deer. In contrast to the deadly properties of misfolded PrP, PrPC seems to possess a neuroprotective activity. More-over, animal models indicated that the stress-protective activity of PrPC and the neurotoxic effects of PrPSc are somehow interconnected. In this timely book, leading scientists in the field have come together to highlight the apparently incongruous activities of different PrP conformers. The articles outline current research on celluar pathways implicated in the formation and signaling of neurotoxic and physiological PrP isoforms and delineate future research direction. Topics covered include the physiologcial activity of PrPC and its possible role as a neurotrophic factor, the finding that aberrant PrP conformers can cause neurodegeneration in the absence of infectious prion propagation, the requirement of the GPI anchor of PrPC for the neurotoxic effects of scrapie prions, the pathways implicated in the formation and neurotoxic properties of cytosolically localized PrP, the impact of metal ions on the processing of PrP, and the role of autophagy in the propagation and clearance of PrPSc. The book is fully illustrated and chapters include comprehensive reference sections. Essential reading for scientists involved in prion research.

## Cyclin Dependent Kinase 5 (Cdk5)

Cyclin Dependent Kinase 5 provides a comprehensive and up-to-date collection of reviews on the discovery, signaling mechanisms and functions of Cdk5, as well as the potential implication of Cdk5 in the treatment of neurodegenerative diseases. Since the identification of this unique member of the Cdk family, Cdk5 has emerged as one of the most important signal transduction mediators in the development, maintenance and fine-tuning of neuronal functions and networking. Further studies have revealed that Cdk5 is also associated with the regulation of neuronal survival during both developmental stages and in neurodegenerative diseases. These observations indicate that precise control of Cdk5 is essential for the regulation of neuronal survival. The pivotal role Cdk5 appears to play in both the regulation of neuronal survival and synaptic functions thus raises the interesting possibility that Cdk5 inhibitors may serve as therapeutic treatment for a number of neurodegenerative diseases.

## Polyglutamine Disorders

This book provides a cutting-edge review of polyglutamine disorders. It primarily focuses on two main aspects: (1) the mechanisms underlying the pathologies' development and progression, and (2) the therapeutic strategies that are currently being explored to stop or delay disease progression. Polyglutamine (polyQ) disorders are a group of inherited neurodegenerative diseases with a fatal outcome that are caused by an abnormal expansion of a coding trinucleotide repeat (CAG), which is then translated in an abnormal protein with an elongated glutamine tract (Q). To date, nine polyQ disorders have been identified and described: dentatorubral-pallidoluysian atrophy (DRPLA); Huntington's disease (HD); spinal–bulbar muscular atrophy (SBMA); and six spinocerebellar ataxias (SCA 1, 2, 3, 6, 7, and 17). The genetic basis of polyQ disorders is well established and described, and despite important advances that have opened up the possibility of generating genetic models of the disease, the mechanisms that cause neuronal degeneration are still largely unknown and there is currently no treatment available for these disorders. Further, it is believed that the different polyQ may share some mechanisms and pathways contributing to neurodegeneration and disease progression.

## Neurons

The brain is the most complex structure that exists in the universe, consisting of neurons whose function is to receive information through dendrites and transmit information through the axon. In neurosciences one of the main problems that exists are neurodegenerative diseases for which until now there has been no cure. This book is mainly focused on updating the information on the signaling process carried out in the development of axons. Topics such as axon guidance and its interaction with the extracellular matrix are discussed. Other important topics are semaphorins and their relationship with neurodegenerative diseases, and the neurobiology of the gap junction in the dorsal root ganglion. Finally, the topic of bioelectrical interfaces destined to regenerate damaged nerves is covered. The information in this book will be very important both for researchers who work with these issues and doctoral students who are involved in neuroscience.

## Drug Design of Zinc-Enzyme Inhibitors

Brings together functional and structural informationrelevant to the design of drugs targeting zinc enzymes The second most abundant transition element in living organisms, zinc spans all areas of metabolism, with zinc-containing proteins offering both established and potential drug targets. Drug Design of Zinc-Enzyme Inhibitors brings together functional and structural information relevant to these zinc-containing targets. With up-to-date overviews of the latest developments field, this unique and comprehensive text enables readers to understand zinc enzymes and evaluate them in a drug design context. With contributions from the leaders of today's research, Drug Design of Zinc-Enzyme Inhibitors covers such key topics as: Major drug targets like carbonic anhydrases, matrix metalloproteinases, bacterial proteases, angiotensin-converting enzyme, histone deacetylase, and APOBEC3G Roles of recently discovered zinc-containing isozymes in cancer, obesity, epilepsy, pain management, malaria, and other conditions Cross reactivity of zinc-enzyme inhibitors and activators The extensive use of X-ray crystallography and QSAR studies for understanding zinc-containing proteins Clinical applications An essential resource for the discovery and development of new drug molecules, Drug Design of Zinc-Enzyme Inhibitors gives researchers, professionals, students, and academics the foundation to understand and work with zinc enzyme inhibitors and activators.

## Protein Folding Disorders Of The Central Nervous System

This exciting new book explores the dark side of the molecular protein assembly bringing an updated view of how failures in the homeostatic mechanisms that efficiently regulate protein folding leads to the accumulation of structurally abnormal pathogenic assemblies, encompassing an emerging group of diseases collectively known as "Protein Folding Disorders." This complex and diverse group of chronic and progressive entities are bridged together by their relationship to structural transitions in the native state of specific proteinaceous components, which for reasons poorly understood, convert into polymeric aggregates that generate poorly soluble tissue deposits and which are considered today the culprit of the disease pathogenesis in their respective diseases. Despite the diversity in the amino acid sequence of the different proteins involved in these heterogeneous disorders, all the pathologic conformers can trigger cascades of events ultimately resulting in cell dysfunction and death with devastating clinical consequences in many of the most precious aspects of human existence including personality, cognition, memory, and skilled movements. This book, which is composed of a compilation of chapters authored by outstanding and well-published scientists in the respective fields currently

performing active investigations at world renowned universities and research centers, focuses on the growing number of diseases associated with protein misfolding in the central nervous system. Individual chapters are dedicated to the most common neurodegenerative diseases associated with protein aggregation/fibrillization focusing on the nature of the pathogenic species and the cellular pathways involved in the molecular pathogenesis of Alzheimer's, Parkinson's, and Huntington's diseases as well as in Amyotrophic Lateral Sclerosis, and Prion disorders. A group of contributions is centered on the current knowledge of the intracellular pathways and subcellular organelles affected by the different disease conditions, while others are focused in the emerging pathogenic role of misfolded subunits assembled into neurotoxic soluble oligomers, and in the novel notion of the transmissibility of the protein misfolded species, an innovative concept until recently only accepted for Prion diseases. Lastly, a different set of chapters is dedicated to the evaluation of novel therapeutic strategies for these devastating diseases. Contents: Misfolding, Aggregation, and Amyloid Formation: The Dark Side of Proteins (Agueda Rostagno and Jorge A Ghiso)Oligomers at the Synapse: Synaptic Dysfunction and Neurodegeneration (Emily Vogler, Matthew Mahavongtrakul, and Jorge Busciglio)Prion-Like Protein Seeding and the Pathobiology of Alzheimer's Disease (Lary C Walker)The Tau Misfolding Pathway to Dementia (Alejandra D Alonso, Leah S Cohen, and Viktoriya Morozova)The Biology and Pathobiology of ±Synuclein (Joel C Watts, Anurag Tandon, and Paul E Fraser)Impact of Loss of Proteostasis on Central Nervous System Disorders (Sentiljana Gumeni, Eleni N Tsakiri, Christina-Maria Cheimonidi, Zoi Evangelakou, Despoina Gianniou, Kostantinos Tallas, Eleni-Dimitra Papanagnou, Aimilia D Sklirou, and Ioannis P Trougakos)Protein Misfolding and Mitochondrial Dysfunction in Amyotrophic Lateral Sclerosis (Giovanni Manfredi and Hibiki Kawamata)Impact of Mitostasis and the Role of the Anti-Oxidant Responses on Central Nervous System Disorders (Sentiljana Gumeni, Eleni N Tsakiri, Christina-Maria Cheimonidi, Zoi Evangelakou, Despoina Gianniou, Kostantinos Tallas, Eleni-Dimitra Papanagnou, Aimilia D Sklirou, and Ioannis P Trougakos)Propagation of Misfolded Proteins in Neurodegeneration: Insights and Cautions from the Study of Prion Disease Prototypes (Robert C C Mercer, Nathalie Daude,

## Alzheimer's Disease

Alzheimer’s disease is an increasingly common form of dementia and despite rising interest in discovery of novel treatments and investigation into aetiology, there are no currently approved treatments that directly tackle the causes of the condition. Due to its multifactorial pathogenesis, current treatments are directed against symptoms and even precise diagnosis remains difficult as the majority of cases are diagnosed symptomatically and usually confirmed only by autopsy. Alzheimer’s Disease: Recent Findings in Pathophysiology, Diagnostic and Therapeutic Modalities provides a comprehensive overview from aetiology and neurochemistry to diagnosis, evaluation and management of Alzheimer's disease, and latest therapeutic approaches. Intended to provide an introduction to all aspects of the disease and latest developments, this book is ideal for students, postgraduates and researchers in neurochemistry, neurological drug discovery and Alzheimer’s disease.

## Etiology of Parkinson's Disease

This comprehensive reference provides a detailed overview of current concepts regarding the cause of Parkinson's disease-emphasizing the issues involved in the design, implementation, and analysis of epidemiological studies of parkinsonism.

## Protein Deimination in Human Health and Disease

Published in 2014, Protein Deimination in Human Health and Disease was the first book on this novel post-translational modification, in which selected positively-charged arginine amino acids are converted to neutral citrulline amino acids by the peptidyl-arginine deiminase (PAD) family of enzymes. This area of research continues to expand rapidly, necessitating the need for this second edition. Chronicling the latest inflammatory, epigenetic, neurodegenerative, and carcinogenic processes, Protein Deimination in Human Health and Disease, Second Edition, updates the latest advances in deimination research, including new information on PAD enzyme structure and activity, and how PAD knock-out animals are being used to study known and newly-discovered links to various human diseases. The first edition outlined what was known about citrullinated proteins in normal tissues such as skin and hair, as well as in maladies such as rheumatoid arthritis (RA), multiple sclerosis (MS), Alzheimer’s disease (AD), glaucoma, peripheral nerve injury, neonatal hypoxic brain damage, and breast cancer. This second edition addresses numerous additional disorders such as diabetes, asthma, traumatic brain

injury, inflammatory bowel disease, lupus, bone disease, heart failure, fronto-temporal dementia, and prostate and colon cancer. It also provides updates on the deimination research covering the three seminal diseases first linked to this process (RA, MS and AD), and details how auto-antibodies against citrullinated proteins contribute to disease. In addition, new hypotheses on the possible pathologic mechanisms of citrullinated myelin basic protein and glial fibrillary acidic protein are also proposed. This second edition also outlines the latest developments in therapeutic strategies, including the use of new PAD antagonists and innovative techniques such as micro-vescicles and stem cells as possible mechanisms to treat these conditions.

## Frontiers in Protein Structure, Function, and Dynamics

This book discusses a broad range of basic and advanced topics in the field of protein structure, function, folding, flexibility, and dynamics. Starting with a basic introduction to protein purification, estimation, storage, and its effect on the protein structure, function, and dynamics, it also discusses various experimental and computational structure determination approaches; the importance of molecular interactions and water in protein stability, folding and dynamics; kinetic and thermodynamic parameters associated with protein-ligand binding; single molecule techniques and their applications in studying protein folding and aggregation; protein quality control; the role of amino acid sequence in protein aggregation; muscarinic acetylcholine receptors, antimuscarinic drugs, and their clinical significances. Further, the book explains the current understanding on the therapeutic importance of the enzyme dopamine beta hydroxylase; structural dynamics and motions in molecular motors; role of cathepsins in controlling degradation of extracellular matrix during disease states; and the important structure-function relationship of iron-binding proteins, ferritins. Overall, the book is an important guide and a comprehensive resource for understanding protein structure, function, dynamics, and interaction.

## Neuroprotection

Neurological disease affects nearly 25%–30% of the world’s population, exerting enormous financial strain on the healthcare system. Estimated current costs are around $800 annual billion, and this number is expected to increase exponentially as the global population ages. As such, new and alternative neuroprotective strategies are urgently needed. This book examines some of the most promising approaches in neuroprotection as well as discusses current goals and prospects. Organized into three sections, chapters cover such topics as the use of cannabinoids, medicinal plants, and essential oils in Alzheimer’s and Parkinson’s; protein misfolding and the neuroprotective potential of vitamin E in cerebral ischemia; and potential new neurological treatments and their mechanisms of action.

## Textbook of Neural Repair and Rehabilitation

Volume 1 of the Textbook of Neural Repair and Rehabilitation covers the basic sciences relevant to recovery of function following injury to the nervous system.

## Brain Disorders in Critical Illness

Brain dysfunction is a major clinical problem in intensive care, with potentially debilitating long-term consequences for post-ICU patients of any age. The resulting extended length of stay in the ICU and post-discharge cognitive dysfunction are now recognized as major healthcare burdens. This comprehensive clinical text provides intensivists and neurologists with a practical review of the pathophysiology of brain dysfunction and a thorough account of the diagnostic and therapeutic options available. Initial sections review the epidemiology, outcomes, relevant behavioral neurology and biological mechanisms of brain dysfunction. Subsequent sections evaluate the available diagnostic options and preventative and therapeutic interventions, with a final section on clinical encephalopathy syndromes encountered in the ICU. Each chapter is rich in illustrations, with an executive summary and a helpful glossary of terms. Brain Disorders in Critical Illness is a seminal reference for all physicians and neuroscientists interested in the care and outcome of severely ill patients.

## Drug Discovery Approaches for the Treatment of Neurodegenerative Disorders

Drug Discovery Approaches for the Treatment of Neurodegenerative Disorders: Alzheimer’s Disease examines the drug discovery process for neurodegenerative diseases by focusing specifically on Alzheimer’s Disease and illustrating the paradigm necessary to ensure future research and treatment

success. The book explores diagnosis, epidemiology, drug discovery strategies, current therapeutics, and much more to provide a holistic approach to the discovery, development, and treatment of Alzheimer's Disease. Through its coverage of the latest research in targeted drug design, preclinical studies, and mouse and rat models, the book is a must-have resource for all pharmaceutical scientists, pharmacologists, neuroscientists, and clinical researchers working in this area. It illustrates why these drugs tend to fail at the clinical stage, and examines Alzheimer's Disease within the overall context of improving the drug discovery process for the treatment of other neurodegenerative disorders. Provides a compilation of chemical considerations required in drug discovery for the treatment of neurodegenerative disorders Examines different classes of compounds currently being used in discovery and development stages Explores in vitro and in vivo models with respect to their ability to translate these models to human conditions Distills the most significant information across multiple areas of Alzheimer's disease research to provide a single, comprehensive, and balanced resource

## Proteostasis and Disease

This book, written by members of the European network PROTEOSTASIS, provides an up-to-date review of the research regarding protein homeostasis in health and disease. With new discoveries contributing to the increasing complexity of this topic, the book offers a detailed overview of the pathways regulating protein homeostasis, including autophagy and the ubiquitin protein family. Following a basic introduction, it explains how defects in protein homeostasis contribute to numerous pathologies, including cancer, neurodegeneration, inflammation and a number of rare diseases. In addition, it discusses, the role of protein homeostasis in cellular development and physiology. Highlighting the latest research in the field of protein homeostasis and its implications for various clinically relevant diseases, the book appeals to researchers and clinicians, while also offering a reference guide for scholars who are new to the field.

## Neurodegenerative Diseases

The editor of this volume, having research interests in the field of ROS production and the damage to cellular systems, has identified a number of enzymes showing ·OH scavenging activities details of which are anticipated to be published in the near future as confirmatory experiments are awaited. It is hoped that the information presented in this book on NDs will stimulate both expert and novice researchers in the field with excellent overviews of the current status of research and pointers to future research goals. Clinicians, nurses as well as families and caregivers should also benefit from the material presented in handling and treating their specialised cases. Also the insights gained should be valuable for further understanding of the diseases at molecular levels and should lead to development of new biomarkers, novel diagnostic tools and more effective therapeutic drugs to treat the clinical problems raised by these devastating diseases.

## Oxidative Stress and Neurodegenerative Disorders

Oxidative stress is the result of an imbalance in pro-oxidant/antioxidant homeostasis that leads to the generation of toxic reactive oxygen species. Brain cells are continuously exposed to reactive oxygen species generated by oxidative metabolism, and in certain pathological conditions defense mechanisms against oxygen radicals may be weakened and/or overwhelmed. DNA is a potential target for oxidative damage, and genomic damage can contribute to neuropathogenesis. It is important therefore to identify tools for the quantitative analysis of DNA damage in models on neurological disorders. This book presents detailed information on various neurodegenerative disorders and their connection with oxidative stress. This information will provide clinicians with directions to treat these disorders with appropriate therapy and is also of vital importance for the drug industries for the design of new drugs for treatment of degenerative disorders. * Contains the latest information on the subject of neurodegenerative disorders * Reflects on various factors involved in degeneration and gives suggestions for how to tackle these problems

## Protein Homeostasis

Proper folding of proteins is crucial for cell function. Chaperones and enzymes that post-translationally modify newly synthesized proteins help ensure that proteins fold correctly, and the unfolded protein response functions as a homeostatic mechanism that removes misfolded proteins when cells are stressed. This book covers the entire spectrum of proteostasis in healthy cells and the diseases that result when control of protein production, protein folding, and protein degradation goes awry.

## Autophagy: Cancer, Other Pathologies, Inflammation, Immunity, Infection, and Aging

Autophagy: Cancer, Other Pathologies, Inflammation, Immunity, Infection, and Aging is an eleven volume series that discusses in detail all aspects of autophagy machinery in the context of health, cancer, and other pathologies. Autophagy maintains homeostasis during starvation or stress conditions by balancing the synthesis of cellular components and their deregulation by autophagy. This series discusses the characterization of autophagosome-enriched vaccines and its efficacy in cancer immunotherapy. Autophagy serves to maintain healthy cells, tissues, and organs, but also promotes cancer survival and growth of established tumors. Impaired or deregulated autophagy can also contribute to disease pathogenesis. Understanding the importance and necessity of the role of autophagy in health and disease is vital for the studies of cancer, aging, neurodegeneration, immunology, and infectious diseases. Comprehensive and forward-thinking, these books offer a valuable guide to cellular processes while also inciting researchers to explore their potentially important connections. Presents the most advanced information regarding the role of the autophagic system in life and death Examines whether autophagy acts fundamentally as a cell survivor or cell death pathway or both Introduces new, more effective therapeutic strategies in the development of targeted drugs and programmed cell death, providing information that will aid in preventing detrimental inflammation Features recent advancements in the molecular mechanisms underlying a large number of genetic and epigenetic diseases and abnormalities, including atherosclerosis and CNS tumors, and their development and treatment Includes chapters authored by leaders in the field around the globe—the broadest, most expert coverage available

## Autophagosome and Phagosome

Autophagy and phagocytosis are distinct yet partially morphologically similar processes. Understanding them is vital for the studies of cancer, aging, neurodegeneration, immunology, and infectious diseases. This book presents autophagosome and phagosome methods for novices and advanced researchers alike. Comprehensive and forward-thinking, the book offers a valuable guide to both cellular processes while inciting researchers to explore their potentially important connections.

## Systems Biology of Free Radicals and Antioxidants

The focus of this collection of illustrated reviews is to discuss the systems biology of free radicals and anti-oxidants. Free radical induced cellular damage in a variety of tissues and organs is reviewed, with detailed discussion of molecular and cellular mechanisms. The collection is aimed at those new to the field, as well as clinicians and scientists with long standing interests in free radical biology. A feature of this collection is that the material also brings insights into various diseases where free radicals are thought to play a role. There is extensive discussion of the success and limitations of the use of antioxidants in several clinical settings.

## Glutamine Repeats and Neurodegenerative Diseases

This book focuses on the discovery of a common genetic basis for a group of inherited neurological disorders, including Huntington's Disease, spino-bulbar atrophy and a series of hereditary ataxias. This shared molecular background and other similarities have led to the development of theoretical models for the pathogenesis of these diseases. It is now also clear that the mechanisms involved are likely to be of more general relevance, outside of this particular group of disorders, with implications for other neurodegenerative processes such as those involved in Alzheimer's, Parkinson's and Prion diseases. The book is an edited and updated compilation evolving from a Royal Society discussion meeting

## Proteopathic Seeds and Neurodegenerative Diseases

The misfolding and aggregation of specific proteins is an early and obligatory event in many of the age-related neurodegenerative diseases of humans. The initial cause of this pathogenic cascade and the means whereby disease spreads through the nervous system, remain uncertain. A recent surge of research, first instigated by pathologic similarities between prion disease and Alzheimer's disease, increasingly implicates the conversion of disease-specific proteins into an aggregate-prone b-sheet-rich state as the prime mover of the neurodegenerative process. This prion-like corruptive protein templating or seeding now characterizes such clinically and etiologically diverse neurological disorders as Alzheimer  s disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and frontotemporal lobar degeneration. Understanding the misfolding, aggregation, trafficking and pathogenicity of the affected proteins could therefore reveal universal pathomechanistic principles for some of the most devastating and intractable human brain disorders. It is time to accept that the prion concept is no longer confined to prionoses but is a promising concept for the understanding and treatment of a remarkable variety of diseases that afflict primarily our aging society.

## Protein Aggregation and Fibrillogenesis in Cerebral and Systemic Amyloid Disease

This volume of the Subcellular Biochemistry series is the result of the long-standing research interest of the editor in the molecular mechanism underlying Alzheimer's disease and other amyloid diseases, indicated also by the earlier book in the series (Volume 38), devoted to Alzheimer's disease. The broad coverage within the present amyloidogenesis book represents an attempt to collate current knowledge relating to the proteins and peptides involved in most of the known amyloid diseases, together with some amyloid/fibril-forming proteins and peptides that are not involved in diseases. Thus, the range of topics included is comprehensive and furthermore it was thought appropriate to include both basic science and clinical presentation of the subjects under discussion.

## Hypoxia and Human Diseases

This book contains a total of 21 chapters, each of which was written by experts in the corresponding field. The objective of this book is to provide a comprehensive and updated overview of cellular and molecular mechanisms underlying hypoxia's impacts on human health, as well as current advances and future directions in the detection, recognition, and management of hypoxia-related disorders. This collection of articles provides a clear update in the area of hypoxia research for biomedical researchers, medical students, nurse practitioners, and practicing clinicians in the fields of high altitude biology, cardiovascular biology and medicine, tumor oncology, obstetrics, pediatrics, and orthodontics and for others who may be interested in hypoxia.

## Dancing Protein Clouds: Intrinsically Disordered Proteins in the Norm and Pathology

"Dancing protein clouds: Intrinsically disordered proteins in the norm and pathology" represents a set of selected studies on a variety of research topics related to intrinsically disordered proteins. Topics in this update include structural and functional characterization of several important intrinsically disordered proteins, such as 14-3-3 proteins and their partners, as well as proteins from muscle sarcomere; representation of intrinsic disorder-related concept of protein structure-function continuum; discussion of the role of intrinsic disorder in phenotypic switching; consideration of the role of intrinsically disordered proteins in the pathogenesis of neurodegenerative diseases and cancer; discussion of the roles of intrinsic disorder in functional amyloids; demonstration of the usefulness of the analysis of translational diffusion of unfolded and intrinsically disordered proteins; consideration of various computational tools for evaluation of functions of intrinsically disordered regions; and discussion of the role of shear stress in the amyloid formation of intrinsically disordered regions in the brain. Provides some recent studies on the intrinsically disordered proteins and their functions, as well as on the involvement of intrinsically disordered proteins in pthogenesis of various diseases Contains numerous illustrative materials (color figures, diagrams, and tables) to help the readers to delve in the information provided Includes contributions from recognized experts in the field