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REVIEW

Role of autophagy and proteostasis in neurodegenerative diseases: Exploring the therapeutic interventions

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Abstract

Neurodegenerative disorders are devastating disorders characterized by gradual loss of neurons and cognition or mobility impairment. The common pathological features of these diseases are associated with the accumulation of misfolded or aggregation of proteins. The pivotal roles of autophagy and proteostasis in maintaining cellular health and preventing the accumulation of misfolded proteins, which are associated with neurodegenerative diseases like Huntington's disease (HD), Alzheimer's disease (AD), and Parkinson's disease (PD). This article presents an in-depth examination of the interplay between autophagy and proteostasis, highlighting how these processes cooperatively contribute to cellular homeostasis and prevent pathogenic protein aggregate accumulation. Furthermore, the review emphasises the potential therapeutic implications of targeting autophagy and proteostasis to mitigate neurodegenerative diseases. While advancements in research hold promise for developing novel treatments, the article also addresses the challenges and complexities associated with modulating these intricate cellular pathways. Ultimately, advancing understanding of the underlying mechanism of autophagy and proteostasis in neurodegenerative disorders provides valuable insights into potential therapeutic avenues and future research directions.

KEYWORDS

cellular homeostatis, neurodegenerative disorders, pathogenesis, proteostasis

1 | INTRODUCTION

Neurodegenerative diseases are devastating cognitive disorders that affect the nervous system, leading to a progressive loss of neuron cells and, consequently, the decline in central nervous system (CNS) functions. The most severe neurodegenerative conditions include Alzheimer's disease (AD), Huntington's disease (HD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and others (Wilson et al., 2023). The common pathological features of these diseases are associated with the accumulation of misfolded or aggregation of proteins. However, some neurodegenerative diseases result from genetic mutations known as autosomal recessive or dominant types (Shang et al., 2022). The treatment for these diseases is immensely challenging, and most therapeutics provide symptomatic relief. Thus, disruption of protein homeostasis, or proteostasis, is a critical player in neurodegenerative diseases. Protein homeostasis refers to the cellular mechanism for the accurate folding, trafficking and clearance of proteins (Höhn et al., 2020). The unwanted proteins that hamper protein homeostasis should be superfluous rapidly.

Additionally, due to environmental stresses such as UV irradiation and reactive oxygen species, cells may

