Combatting Proteostasis Imbalance in Age-Related Neurodegenerative Disorders: Targeted Modulation of Molecular Chaperone Networks

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Abstract. Proteostasis imbalance is a hallmark of age-related neurodegenerative diseases. This study investigates the modulation of molecular chaperone networks to restore proteostasis in cellular models of Alzheimer's and Parkinson's diseases. Using cutting-edge CRISPR-Cas9 gene editing and proteomics, we identified key chaperones capable of ameliorating protein misfolding. The results demonstrate that targeted chaperone modulation can significantly reduce proteotoxic stress, offering insights into therapeutic strategies for neurodegeneration.

Keywords: Proteostasis, Neurodegeneration, Molecular Chaperones, CRISPR-Cas9, Protein Misfolding, Alzheimer's Disease, Parkinson's Disease

Introduction

The global burden of neurodegenerative disorders, notably Alzheimer's and Parkinson’s diseases, is escalating with the aging population, necessitating advanced therapeutic strategies. One of the primary molecular underpinnings of these disorders is proteostasis imbalance, characterized by the accumulation of misfolded proteins leading to cellular dysfunction and neurodegeneration. Traditional therapeutic approaches have largely focused on symptomatic relief, often neglecting the root molecular disruptions. Recent advancements in molecular biology have highlighted the critical role of chaperone proteins in maintaining proteostasis by facilitating the correct folding and degradation of misfolded proteins. This study leverages the potential of molecular chaperones to combat the proteostasis imbalance in neurodegenerative diseases. Utilizing CRISPR-Cas9 for precise gene editing and advanced proteomics, we dissect the chaperone networks altered in cellular models of Alzheimer's and Parkinson's diseases. We propose that targeted

modulation of these networks can restore proteostasis and alleviate neurodegenerative progression. The paper is structured as follows: First, we elucidate the methodologies employed in chaperone identification. Subsequently, we present the findings on chaperone efficacy in mitigating proteotoxic stresses. Finally, we discuss the implications of these findings for therapeutic development.

References

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