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Epigenetic Regulation of Gene Expression in the Development of Neurodegenerative Diseases: A Narrative Review

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ABSTRACT

Neurodegenerative diseases have a significant impact on individuals and society. The exact causes of these diseases are not fully understood, but evidence suggests that a combination of genetic, environmental, and lifestyle factors contribute to their development. Methods: This narrative review explores the role of epigenetic regulation in gene expression during the development of neurodegenerative diseases. An exhaustive literature search was conducted using electronic databases, and articles focusing on epigenetic regulation in the context of neurodegenerative diseases were selected for analysis. Epigenetic mechanisms, including DNA methylation, histone modifications, and non-coding RNA molecules, play a crucial role in regulating gene activity and have significant implications for cellular function and disease development. Abnormal DNA methylation patterns have been associated with neurological disorders and neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease. Histone modifications have also been implicated in the regulation of gene expression in neurodegenerative diseases. Non-coding RNAs, including microRNAs and long non-coding RNAs, are involved in gene expression regulation and have been found to be dysregulated in neurodegenerative diseases. Conclusion: Understanding the role of epigenetics in neurodegenerative diseases offers insights into disease development and progression. It provides opportunities for the development of potential therapeutic strategies that target epigenetic modifications. However, studying epigenetic changes in neurodegenerative diseases presents challenges, including the complexity of epigenetic regulation and the heterogeneity of the diseases. Nonetheless, the therapeutic potential of epigenetic regulation in neurodegenerative diseases is promising, with potential strategies including DNA methylation modifiers, histone deacetylase inhibitors, microRNA-based therapies, lncRNA modulation, and epigenetic diets. Continued research is needed to further understand the underlying mechanisms and develop safe and effective treatments for neurodegenerative diseases.

KEYWORDS: Epigenetics, Gene expression, Neurodegenerative diseases, Epigenetic regulation, DNA methylation, Histone modifications, Transcriptional regulation, Neurodevelopment.

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INTRODUCTION

Neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis (ALS), are characterized by the progressive degeneration of neurons in the central nervous system. These diseases have a significant impact on individuals and society, making them an important area of study in the medical field. (Emard et al., 1995).

The high prevalence of neurodegenerative diseases, especially among the elderly population in industrialized countries, contributes to their importance in medicine. They are a major cause of disability and mortality, posing significant challenges in terms of diagnosis, treatment and management. (Emard et al., 1995).

The exact causes of neurodegenerative diseases are not fully understood, but there is evidence to suggest that a combination of genetic, environmental and lifestyle factors contribute to their development. Research has focused on identifying risk factors and possible protective factors associated with these diseases. For example, exposure to toxins and deficiencies in elements such as calcium and selenium have been linked to an increased risk of developing neurodegenerative diseases. (Emard et al., 1995). In addition, associations have been observed between neurodegenerative

diseases and conditions such as malignancies and sleep disorders. (Nozaki et al., 2014), (Lin et al., 2023).

Understanding the underlying mechanisms and risk factors associated with neurodegenerative diseases is crucial for the development of effective prevention strategies, diagnostic tools, and therapeutic interventions. Researchers have explored the potential role of various factors, including metals, inflammation and physical activity, in the development and progression of these diseases. (Cicero et al., 2017a), (Liao et al., 2022), (Wu et al., 2021).

Epigenetics, defined as the study of changes in gene expression that do not involve alterations in DNA sequence, is highly relevant to understanding the molecular basis of neurodegenerative diseases. Epigenetic modifications, including DNA methylation, histone modifications, and non-coding RNA molecules, play a crucial role in regulating gene activity and have significant implications for cell function and disease development. (Rasmi et al., 2023).

Numerous studies have shown the involvement of epigenetic mechanisms in neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and Huntington's disease. For example, oxidative stress, a known contributor to neurodegeneration, has been shown to induce epigenetic modifications, including DNA oxidation and histone modifications, which can lead to altered gene expression patterns associated with disease pathophysiology. (Yaribeygi et al., 2018).

In addition, exposure to certain metals, such as lead and mercury, can induce oxidative stress and alter epigenetic marks, thus contributing to neurotoxicity and neurodegeneration. (Cicero et al., 2017b). Epigenetic changes have also been implicated in the regulation of genes involved in neuroinflammation, protein aggregation and mitochondrial dysfunction, which are key processes in neurodegenerative diseases. (Rasmi et al., 2023).

Understanding the role of epigenetics in neurodegenerative diseases offers insights into the underlying mechanisms of disease development and progression. It provides opportunities for the development of potential therapeutic strategies that target epigenetic modifications. For example, DNA methylation inhibitors and histone deacetylase inhibitors have shown promise as potential therapeutic agents for neurological disorders. (Rasmi et al., 2023). In addition, the goal of reducing oxidative stress and modulating epigenetic marks has potential as a therapeutic approach for neurodegenerative diseases. (Yaribeygi et al., 2018), (Cicero et al., 2017b)

METHODOLOGY

The aim of this narrative review was to explore the role of epigenetic regulation in gene expression during the development of neurodegenerative diseases.

Literature search: An exhaustive literature search was conducted using electronic databases, including PubMed, as well as other relevant sources. The search aimed to identify articles published from the earliest available date to the present, ensuring a comprehensive understanding of the topic.

Search strategy: The search strategy included the use of appropriate keywords and their combinations, such as:

Epigenetic regulation, Gene expression, Neurodegenerative diseases

The inclusion criteria for the selection of articles were as follows:

Studies that focus on the epigenetic regulation of gene expression in the context of neurodegenerative diseases. Research involving human subjects or animal models. Studies that provide information on DNA methylation, histone modifications, or other mechanisms of epigenetic regulation. There are all articles published in English.

The exclusion criteria were as follows:

Studies not related to epigenetic regulation or gene expression in the context of neurodegenerative diseases and studies conducted in non-human subjects or in in vitro models and articles that did not provide relevant data or information on specific epigenetic regulatory mechanisms.

Two independent reviewers assessed articles based on their titles and abstracts. Any discrepancies were resolved by discussion and, if no consensus was reached, a third reviewer was consulted. Full articles meeting the inclusion criteria were obtained for detailed analysis.

Data extraction and synthesis: Data from selected articles were extracted and synthesized to identify common themes and patterns related to epigenetic regulation of gene expression in neurodegenerative diseases. Key findings and ideas related to DNA methylation, histone modifications, and other epigenetic mechanisms were analyzed and summarized.

Discussion and conclusion: The findings of this narrative review were discussed among the authors to identify significant findings and potential implications. The review provides a comprehensive understanding of the role of epigenetic regulation in gene expression during the development of neurodegenerative diseases. The synthesized data will contribute to scientific knowledge and inspire future research in this field.

RESULTS

Epigenetic mechanisms and gene regulation

DNA methylation

DNA methylation is an epigenetic mechanism involving the addition of a methyl group to the DNA molecule in cytosine residues in CpG dinucleotides. This modification is catalyzed by DNA methyltransferase enzymes. DNA methylation can have various effects on gene expression, depending on its location within the genome. DNA methylation in gene-promoting regions is generally associated with gene repression by preventing the binding of transcription factors and other regulatory proteins, inhibiting gene transcription. On the other hand, DNA methylation in regions of the gene may be associated with active gene expression. DNA methylation patterns are established during early

development and can be influenced by environmental factors throughout life. Changes in DNA methylation patterns can have significant impacts on gene regulation and contribute to disease development and progression. (Rasmi et al., 2023), (Silva & Kamens, 2021).

Understanding the role of DNA methylation in gene regulation is essential for unraveling the complexities of various biological processes and diseases. Abnormal patterns of DNA methylation have been associated with a wide range of conditions, including neurological disorders, cancer, and autoimmune diseases. Changes in DNA methylation in neurological disorders and neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease, can affect the expression of genes involved in neurodegeneration. In cancer, alterations in DNA methylation can lead to repression of tumor suppressor genes or activation of oncogenes, contributing to tumor development and progression. (Rasmi et al., 2023), (Silva & Kamens, 2021), (Braun et al., 2016).

Several studies have investigated the relationship between DNA methylation and neurodegenerative diseases. Study explored DNA methylation patterns associated with Huntington's disease and identified potential epigenetic markers for disease progression (Alvarado-Cruz et al., 2018). In addition, a meta-analysis examined changes in DNA methylation in multiple sclerosis and highlighted the possible involvement of epigenetic mechanisms in the development of the disease. (Ning et al., 2022). These studies contribute to our understanding of the complex interaction between DNA methylation and neurodegenerative diseases.

HISTONE MODIFICATIONS

Histone modifications are chemical alterations made to histone proteins, which are critical in packaging DNA into a compact structure known as chromatin. These alterations can have profound effects on gene expression and chromatin structure.

Histones can undergo a variety of modifications, including acetylation, methylation, phosphorylation, ubiquitination, and others. These changes occur in particular amino acids within the tails of histones, which protrude from the nucleus of the nucleosome.

Histone modifications are key players in the regulation of gene expression by enhancing or repressing transcription. For example, histone acetylation is generally associated with gene activation, as it weakens the interaction between DNA and histones, allowing transcription factors and other regulatory proteins to access DNA. In contrast, histone methylation can both activate and repress gene expression depending on the precise amino acid and degree of methylation.

In addition to their role in gene expression, histone modifications also affect chromatin structure. Different combinations of histone modifications can generate different chromatin states, such as eu-chromatin (more open and accessible) or heterochromatin (more condensed and less accessible). These chromatin states can influence DNA's accessibility to transcription factors and other regulatory proteins, which in turn influences gene expression.

In general, histone modifications are essential for precise control of gene expression and maintenance of chromatin structure. By adjusting these modifications, cells can determine which genes are turned on or off in response to various developmental signals and signals. Understanding the role of histone modifications is crucial to unraveling the complex mechanisms underlying epigenetics and various diseases (Alaskhar Alhamwe et al., 2018), (Dik et al., 2012), (F. Li et al., 2018).

Several studies have pointed to the role of histone modifications in the development and progression of neurodegenerative diseases. For example:

Alzheimer's disease: Changes in histone acetylation and methylation patterns have been observed in Alzheimer's disease. Hyperacetylation of H3 and H4 histones has been reported in the promoter of the BACE1 gene, a gene essential for the production of amyloid beta peptide (Lopez del Amo et al., 2012). In addition, altered histone methylation, especially in histone H3, has been associated with dysregulation of genes related to Alzheimer's disease. (Shamaei et al., 2013).

Huntington's disease: The mutation in the huntingtin gene seen in Huntington's disease can lead to abnormal interactions with several proteins, including those involved in histone acetylation and methylation. These interactions could potentially alter histone modification patterns and contribute to disease progression. (El-Agnaf et al., 2017).

Parkinson's disease: Histone modifications have also been implicated in Parkinson's disease. For example, a decrease in histone H3 acetylation and an increase in histone H3 methylation in lysine 9 have been reported in models of Parkinson's disease. (Wei et al., 2014). These histone modifications could affect gene expression and contribute to neuronal death.

Understanding these histone modifications and their effects on gene expression and cell function may potentially inform the development of novel therapies for neurodegenerative diseases. (Kronenberg & Schwaiger, 2017), (Baltrėnaitė & Baltrėnas, 2019).

Non-coding RNA

Non-coding RNAs (ncRNAs) play a crucial role in epigenetic regulation and gene expression. Epigenetic regulation refers to changes in gene activity that do not involve alterations in the genetic code but are passed on to at least one successive generation. This form of regulation mainly involves changes in the DNA molecule or associated proteins that can influence gene activity.

Long non-coding RNAs (lncRNAs): These are ncRNAs that are more than 200 nucleotides in length. lncRNAs have been shown to regulate gene expression at various levels, including chromatin remodeling, transcription, and post-transcriptional processing. lncRNAs can interact with DNA, RNA, and

proteins to form a complex regulatory network (Azizi et al., 2019).

MicroRNAs (miRNAs): These are small ncRNAs, about 22 nucleotides in length, that can bind to mRNA molecules and prevent their translation into proteins, thereby inhibiting gene expression. MiRNAs play a crucial role in a wide range of biological processes, and their dysregulation has been implicated in various diseases. (Piket et al., 2019).

Circular RNAs (cRNAs): These are a type of RNA that, unlike linear RNAs, form a covalently closed continuous loop. cRNAs can function as miRNA sponges, thereby affecting miRNA-mediated regulation of gene expression. They have been found to be involved in various diseases (Moallemi Rad et al., 2023).

There are known connections between non-coding RNAs (ncRNAs) and the development or progression of neurodegenerative diseases. Noncoding RNAs, which include long noncoding RNAs (lncRNAs) and microRNAs (miRNAs), do not code for proteins but play important roles in regulating gene expression.

In neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD), alterations in the expression levels of certain ncRNAs have been observed. For example, in AD, several lncRNAs have been found to be dysregulated and these changes are thought to contribute to the pathogenesis of the disease. (Chen et al., 2019). In addition, lncRNAs are involved in several aspects of AD, such as beta-amyloid plaque synthesis, neuronal plasticity, inflammation, and apoptosis, which are key features of the disease. (Saleh et al., 2023)

In PD, lncRNAs have also been implicated in disease development and progression. (Chen et al., 2019). Similarly, in multiple sclerosis (MS), a demyelinating disease of the central nervous system, both lncRNAs and miRNAs have been found to be dysregulated. (Jalaiei et al., 2021), (Piket et al., 2019).

Given their role in these neurodegenerative diseases, ncRNAs have been proposed as possible therapeutic targets. In addition, because of their disease-specific expression patterns, ncRNAs are also being explored as potential biomarkers for early disease detection and monitoring of disease progression.

However, although the connections between ncRNAs and neurodegenerative diseases are becoming increasingly clear, more research is needed to fully understand the exact mechanisms by which these ncRNAs contribute to disease development and progression, and determine how they can best be used in clinical settings.

Epigenetic regulation in specific neurodegenerative diseases

Alzheimer's disease

Epigenetic changes are emerging as important contributors to the pathogenesis of Alzheimer's disease (AD). These changes, which include modifications to DNA methylation, modification of histones, and non-coding RNAs, can influence gene expression without changing the DNA sequence itself.

One of the key studies identified altered patterns of DNA methylation associated with Alzheimer's disease. In particular, genes associated with synaptic function and neuroinflammation showed changes in DNA methylation in AD patients compared to controls. (Hohman et al., 2017). However, the exact mechanism by which these epigenetic changes influence disease progression is not yet fully understood.

Modifications of histones, another form of epigenetic change, have also been linked to AD. It was suggested that beta-amyloid, a protein whose abnormal accumulation is a hallmark of AD, could generate abnormal brain activity, possibly through epigenetic mechanisms, influencing the progression of neurodegeneration and cortical excitability. (Nicastro et al., 2016).

Finally, the role of non-coding RNAs in the epigenetic regulation of Alzheimer's disease is increasingly recognized. One study identified glycosylated glyceraldehyde 3-phosphate dehydrogenase (GAPDH) S-glutathione, an unusual modification that is abundant in the blood of AD patients and is thought to correlate with disease progression. (Tsai et al., 2020).

Taken together, these findings suggest that specific epigenetic changes may influence Alzheimer's disease progression by affecting the expression and function of key genes and proteins involved in disease pathogenesis. However, more research is needed to fully elucidate these mechanisms and their potential implications for therapeutic strategies in AD.

PARKINSON'S DISEASE

Epigenetic regulation has a significant impact on the development and progression of Parkinson's disease (PD). These regulatory mechanisms can modulate gene expression without altering the underlying DNA sequence and are influenced by genetic and environmental factors. Numerous studies have highlighted the role of epigenetic changes in the etiology and progression of PD.

A study analyzes the impact of environmental risk factors such as smoking, coffee consumption, pesticide exposure and heavy metal exposure on the development of PD, linking these exposures to epigenetic modifications that could modulate gene expression and cell functions. (Angelopoulou et al., 2022). This suggests that epigenetic alterations could partially mediate the influence of environmental factors on PD risk and progression.

Another review provides a comprehensive overview of the role of epigenetics in the intricate interplay between genetic and environmental factors underlying PD. (Davie, 2008). This review proposes that various epigenetic changes, such as DNA methylation, histone modifications and non-coding RNAs, could mediate the connection between environmental

exposures and genetic susceptibilities, contributing to the multifactorial pathogenesis of PD.

In addition, another study found that levodopa-induced changes in synaptic dopamine levels, a key aspect of PD progression, could be influenced by epigenetic modifications. (de la Fuente-Fernández et al., 2004). Specifically, these epigenetic changes could modulate the therapeutic response to levodopa and the onset of levodopa-induced dyskinesias, a common motor complication in PD.

In summary, epigenetic regulation plays a fundamental role in the development and progression of Parkinson's disease. Several environmental factors can influence epigenetic modifications, which in turn can alter gene expression, thus contributing to the pathogenesis and progression of PD.

Amyotrophic Lateral Sclerosis (ALS) and other neurodegenerative diseases

Epigenetic regulation plays a crucial role in the development and progression of various neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS). Studies have found that epigenetic mechanisms, including DNA methylation, histone modifications, and non-coding RNAs, can have a significant impact on the onset and progression of these diseases. (Rasmi et al., 2023).

In the case of ALS, one study noted that epigenetic "clocks" — tools that estimate an individual's biological age based on DNA methylation patterns — could provide valuable information about the disease's onset, progression, and pathology. (Yang et al., 2023). This could help in the early diagnosis and timely treatment of ALS.

Another study examined the role of environmental factors, specifically metal exposure, in the context of ALS and other neurodegenerative diseases. The findings suggest that these exposures could induce oxidative stress in brain cells, leading to cell death and neurodegeneration, contributing to the development of ALS. (Cicero et al., 2017a).

In addition, epigenetic alterations in other neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease have also been studied. These studies have indicated that changes in DNA methylation, histone modifications, and miRNA expression could contribute to the pathogenesis of these diseases. (Emfietzoglou et al., 2021).

Overall, the role of epigenetic regulation in ALS and other neurodegenerative diseases is an active area of research. Current evidence suggests that epigenetic changes can have a significant impact on disease onset and progression, and a deeper understanding of these mechanisms may provide potential therapeutic targets for these conditions.

Techniques to study epigenetics in neurodegenerative diseases

The study of epigenetic modifications in neurodegenerative diseases involves a combination of techniques and tools from different scientific fields, including molecular biology, genetics, bioinformatics and neurobiology. Some of the most commonly used are:

DNA methylation analysis: Techniques for studying DNA methylation include bisulfite sequencing, which can provide single-nucleotide resolution of methylation status, and methylation-specific PCR (MSP), which can detect methylation changes in specific genes. In addition, DNA methylation profiles can be generated at the genomic level using high-throughput platforms such as Illumina's Infinium MethylationEPIC BeadChip. (Rasmi et al., 2023), (Yang et al., 2023).

Histone modification analysis: Chromatin immunoprecipitation (ChIP) followed by sequencing (ChIP-seq) or quantitative PCR (ChIP-qPCR) is commonly used to study histone modifications, including methylation and acetylation. These techniques can provide information about the location and abundance of specific histone modifications. (Rasmi et al., 2023), (Yang et al., 2023).

Non-coding RNA analysis: Non-coding RNAs, including microRNAs and long non-coding RNAs, are involved in the regulation of gene expression and can be affected by epigenetic changes. RNA sequencing (RNA-seq) and quantitative PCR can be used to measure the expression of these molecules in the context of neurodegenerative diseases (Rasmi et al., 2023), (Yang et al., 2023).

Epigenomic association studies (EWAS): EWAS is a method used to identify genome-wide epigenetic markers that are associated with specific diseases or traits. This approach often uses high-throughput technologies such as DNA methylation microarrays or next-generation sequencing. (Karlsson Linnér et al., 2017).

Bioinformatic analysis: Analysis of the large and complex datasets generated by these techniques often requires sophisticated bioinformatics tools and algorithms. These may include software to analyze sequencing data, tools to identify differentially methylated or expressed regions, and databases to store and access epigenetic and genomic information. (Yang et al., 2023), (Wong et al., 2021).

Pharmacological modulation: To study the functional impact of epigenetic modifications, researchers often use pharmacological agents that can modify these changes, such as DNA methyltransferase inhibitors, histone deacetylase inhibitors, or histone demethylase inhibitors. (Rasmi et al., 2023).

These techniques and tools, often used in combination, allow researchers to gain a comprehensive understanding of the role of epigenetic modifications in the pathogenesis of neurodegenerative diseases and may contribute to the identification of potential therapeutic targets.

Challenges and limitations in the study of epigenetics in neurodegenerative diseases

The study of epigenetic changes in neurodegenerative diseases presents a unique set of challenges and limitations for researchers.

First, the nascent state of epigenetic research in neurodegenerative disorders is a major obstacle. The technology used to detect epigenetic changes is constantly

evolving and understanding the precise epigenetic mechanisms involved in disease development and progression is an ongoing process. (Fenoglio et al., 2018).

In addition, the complexity of epigenetic regulation is another significant challenge. Epigenetic regulation occurs at multiple cellular levels and is influenced by various factors such as aging and environmental cues. Therefore, unraveling how these influences interact and induce epigenetic changes in neurodegenerative diseases requires further investigation. (Fenoglio et al., 2018).

The heterogeneity of neurodegenerative diseases also poses a distinct challenge. Diseases such as Alzheimer's, Parkinson's and Amyotrophic Lateral Sclerosis have unique pathologies and distinct clinical manifestations. (Cicero et al., 2017a). Identifying common epigenetic changes in these diverse diseases and establishing their specific roles in each disease subtype is a complicated task.

Finally, the lack of large-scale, well-structured studies with substantial sample sizes is a limiting factor. Most studies in this field are small-scale or lack sufficient sample sizes, which affects the generalizability of the findings. Many studies also rely on retrospective data or case-control designs, which introduces bias and limits the ability to establish causal relationships. (Yang et al., 2023).

Despite these obstacles, continuous advances in research and technology are gradually revealing the role of epigenetic changes in neurodegenerative diseases, which could lead to the creation of innovative therapeutic strategies. (Fenoglio et al., 2018)

Discussion

In neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis (ALS), alterations in DNA methylation and histone modifications have been observed. These epigenetic changes can influence the expression of genes related to neurodegeneration and contribute to the development of these diseases. (Ao et al., 2022), (Alvarado-Cruz et al., 2018), (And et al., 2022).

Non-coding RNAs (ncRNAs) also play an important role in epigenetic regulation and gene expression. Long non-coding RNAs (lncRNAs) and microRNAs (miRNAs) regulate gene expression at different levels and alterations in their expression have been found in neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease and ALS. (Azizi et al., 2019), (Piket et al., 2019), (Moallemi Rad et al., 2023).

The study of epigenetics in neurodegenerative diseases involves various techniques such as DNA methylation analysis, histone modification analysis, non-coding RNA analysis, and epigenomic association studies. These techniques provide insight into specific epigenetic changes associated with diseases. (Rasmi et al., 2023), (Yang et al., 2023).

Despite advances in epigenetic research in neurodegenerative diseases, there are challenges and limitations in this field. The technology used to detect epigenetic changes is constantly evolving and fully understanding the epigenetic mechanisms in these diseases is an ongoing process. In addition, the complexity of epigenetic regulation and the heterogeneity of neurodegenerative diseases pose challenges for research (Fenoglio et al., 2018), (Cicero et al., 2017a).

DNA

methylation, histone modifications and non-coding RNAs are important epigenetic regulatory mechanisms that play a crucial role in neurodegenerative diseases. These epigenetic changes can influence gene expression and chromatin structure, which in turn can contribute to the development and progression of diseases such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis.

To study epigenetics in neurodegenerative diseases, various techniques are used, such as DNA methylation analysis, histone modification analysis, non-coding RNA analysis and epigenomic association studies. These techniques allow researchers to gain a comprehensive understanding of epigenetic changes and their relationship to diseases.

However, the study of epigenetics in neurodegenerative diseases also presents challenges and limitations. Research in this field is still in its early stages, and more research is needed to fully understand the epigenetic mechanisms involved in these diseases. In addition, the complexity of epigenetic regulation, the heterogeneity of neurodegenerative diseases and the lack of large-scale studies are factors that hinder research.

Despite these challenges, the study of epigenetics in neurodegenerative diseases offers great therapeutic potential. Strategies such as DNA methylation modifiers, histone deacetylase inhibitors, microRNA-based therapies, and long non-coding RNA modulation are being investigated as potential therapeutic approaches. In addition, findings from epigenetic research may lead to more personalized treatments and the development of biomarkers for the diagnosis and prognosis of neurodegenerative diseases.

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