

Review Article



Non-Coding RNA as Biomarkers and Therapeutic Targets in Neurodegenerative Diseases: Mechanistic Insights and Clinical Translation

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Received: 03-06-2026; Revised: 25-08-2026; Accepted: 29-08-2026; Published online: 20-09-2026.

ABSTRACT

Neurodegenerative diseases are characterized by the progressive loss of neurons, leading to disorders such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis (ALS). Although several medications are available, most provide only symptomatic relief and do not stop disease progression. A major challenge in developing effective therapies is the blood–brain barrier (BBB), which restricts the delivery of many therapeutic agents to the brain. Recent advances in RNA-based therapeutics and nanotechnology have created new opportunities for targeted drug delivery and disease management. Non-coding RNAs (ncRNAs), including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), play critical roles in regulating gene expression and have emerged as promising biomarkers for early diagnosis and therapeutic intervention. Nanoparticle-based delivery systems further improve the transport of these molecules across the BBB, enhancing treatment efficiency while minimizing systemic side effects. This article discusses the molecular mechanisms of ncRNAs, their diagnostic and therapeutic potential, and the role of advanced drug delivery strategies in improving the clinical management of neurodegenerative diseases.

Keywords: Non coding RNA, neurodegenerative, biomarkers, RNA therapeutic, miRNA therapeutic.

INTRODUCTION

Neurodegenerative diseases (NDs), including Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Huntington's disease (HD), and several neuropsychiatric disorders, are characterized by the progressive degeneration and loss of neurons and synaptic connections, ultimately resulting in irreversible neurological dysfunction¹. These disorders manifest with distinct clinical features depending on the specific brain regions affected by neuronal loss. The diagnosis of NDs is primarily based on clinical manifestations, supported by neuroimaging techniques such as magnetic resonance imaging (MRI)². The onset, severity, and progression of symptoms are closely associated with the extent and location of neuronal degeneration. For instance, in AD, early neuronal loss predominantly occurs in the hippocampus, a brain region essential for learning and episodic memory, leading to progressive cognitive decline³.

Neuroinflammation has emerged as a central mechanism underlying the pathogenesis of NDs and is currently a major focus of neurodegenerative research. Persistent activation of microglia and astrocytes promotes the release of pro-inflammatory cytokines, chemokines, and reactive oxygen species, thereby exacerbating neuronal injury and disease progression. Consequently, modulation of neuroinflammatory pathways has gained considerable attention as a promising therapeutic strategy for neuroprotection and neurorestoration⁴. Furthermore, accumulating evidence suggests that the interaction between genetic susceptibility and environmental factors

significantly influences neuroinflammatory responses and disease progression. Environmental exposures, including pesticides, heavy metals, and other neurotoxins, have been associated with an increased risk of developing NDs, highlighting the importance of addressing modifiable risk factors. In parallel, genetic alterations, such as mutations in the leucine-rich repeat kinase 2 (LRRK2) gene in PD and the apolipoprotein E (APOE) gene in AD, further contribute to disease susceptibility and progression, emphasizing the complexity of ND pathogenesis⁵.

Classification and Biogenesis of Non-Coding RNAs

MicroRNAs (miRNAs)

MicroRNAs (miRNAs) are small endogenous non-coding RNAs, typically 20–24 nucleotides in length, that play a pivotal role in post-transcriptional gene regulation. They are transcribed from genomic DNA as primary miRNAs (pri-miRNAs), which undergo sequential processing to form precursor miRNAs (pre-miRNAs) and ultimately mature miRNAs. Mature miRNAs regulate gene expression primarily by binding to complementary sequences within the 3' untranslated region (3' UTR) of target messenger RNAs (mRNAs), resulting in mRNA degradation or translational repression. In addition to the 3' UTR, miRNAs have also been reported to interact with the 5' UTR, coding regions, and promoter sequences, thereby influencing gene expression through multiple regulatory mechanisms⁶. Most miRNAs exert their biological functions by negatively regulating target gene expression, making them key modulators of cellular differentiation, proliferation, apoptosis, and immune responses⁷.



Long Non-Coding RNAs (lncRNAs)

Long non-coding RNAs (lncRNAs) are a heterogeneous class of RNA molecules longer than 200 nucleotides that lack protein-coding potential but play essential roles in regulating gene expression at the epigenetic, transcriptional, and post-transcriptional levels. They participate in diverse biological processes by interacting with DNA, RNA, and proteins to regulate chromatin remodeling, transcription, RNA splicing, translation, and intracellular signaling pathways. Many lncRNAs originate from enhancer regions and associate with chromatin-modifying complexes, contributing to tissue-specific gene regulation during development and disease. Their modular structural organization enables interactions with multiple molecular partners, allowing them to function as scaffolds, guides, decoys, or molecular signals. Increasing evidence highlights the involvement of lncRNAs in cellular homeostasis, metabolism, and the pathogenesis of numerous human diseases, including neurodegenerative disorders^{8,9}.

Circular RNAs (circRNAs)

Circular RNAs (circRNAs) are a distinct class of endogenous non-coding RNAs characterized by a covalently closed-loop structure formed through back-splicing of precursor mRNAs. Unlike linear RNAs, circRNAs lack both 5' caps and 3' poly(A) tails, rendering them highly resistant to exonuclease-mediated degradation and therefore exceptionally stable. They regulate gene expression through multiple mechanisms, including acting as microRNA sponges, interacting with RNA-binding proteins, modulating transcription, and in some cases serving as templates for protein translation. Owing to their high stability, evolutionary conservation, and tissue-specific expression patterns, circRNAs have emerged as promising biomarkers and potential therapeutic targets in a wide range of diseases, particularly neurodegenerative disorders^{10,11}. The classification of the non coding RNAs are shown in the figure 1

CLASSIFICATION AND BIOGENESIS OF NON-CODING RNAs

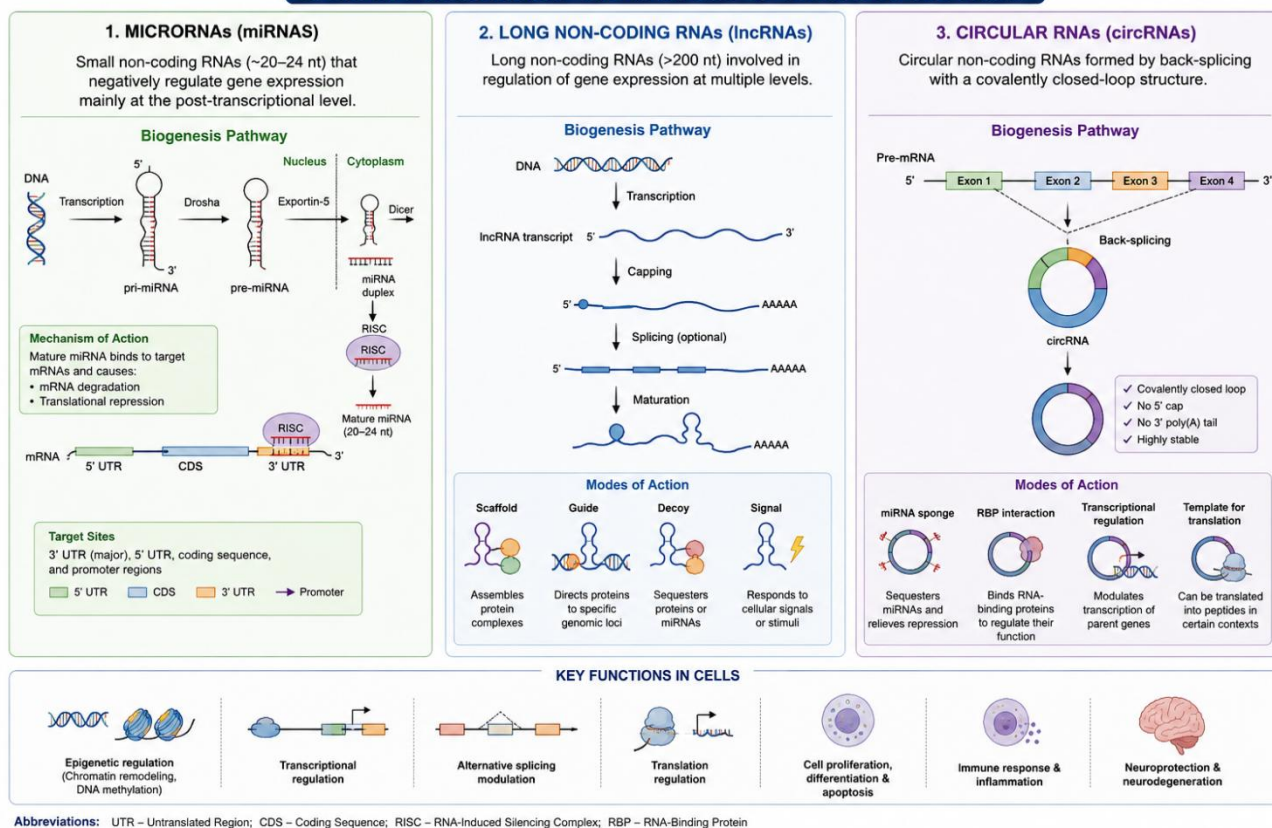


Figure 1: Classification and biogenesis of Non Coding RNAs

Mechanistic Role in Neurodegeneration

Neurodegenerative diseases are characterized by progressive neuronal dysfunction caused by protein aggregation, neuroinflammation, mitochondrial dysfunction, oxidative stress, impaired energy metabolism, and DNA damage, ultimately leading to neuronal death¹².

Protein Misfolding and Aggregation

Protein misfolding and aggregation are central pathological features of many neurodegenerative diseases. Misfolded proteins undergo abnormal conformational changes that promote the formation of toxic aggregates, disrupting neuronal function and survival. Aggregation usually begins with the formation of small protein seeds, which recruit

additional proteins and facilitate the spread of pathological aggregates throughout the nervous system¹³.

Abnormal accumulation of amyloid- β (A β), tau, α -synuclein, and TDP-43 impairs protein homeostasis, intracellular transport, mitochondrial function, and synaptic signaling, thereby accelerating neuronal degeneration. Cellular quality-control mechanisms, including the unfolded protein response (UPR), molecular chaperones, chaperone-mediated autophagy (CMA), autophagy, and the Keap1–Nrf2–ARE pathway, play essential roles in removing misfolded proteins. Dysfunction of these pathways promotes protein accumulation and disease progression, making them attractive therapeutic targets^{14,15}.

Alzheimer's Disease

Alzheimer's disease (AD) is the most common neurodegenerative disorder and the leading cause of dementia in older adults. It is characterized by progressive memory loss, cognitive impairment, and behavioral changes that gradually interfere with daily activities¹⁶. The pathological hallmarks of AD are the accumulation of amyloid- β (A β) plaques and hyperphosphorylated tau neurofibrillary tangles, which impair synaptic function and promote progressive neuronal loss¹⁷.

Diagnosis is based on clinical assessment, cognitive evaluation, and exclusion of other causes of dementia. Neuroimaging and cerebrospinal fluid (CSF) biomarkers may aid early diagnosis. AD is commonly classified into mild, moderate, and severe stages, each associated with progressive cognitive and functional decline¹⁸. Approximately 60–80% of dementia cases worldwide are attributed to AD, making it a major global health concern. Progressive accumulation of A β plaques and tau tangles leads to synaptic dysfunction, neuroinflammation, and neuronal degeneration¹⁹.

Parkinson's Disease

Parkinson's disease (PD) is the second most common neurodegenerative disorder, affecting approximately 1% of individuals over 60 years of age. It is characterized by degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc) and the accumulation of α -synuclein-containing Lewy bodies. Although the exact pathogenesis remains unclear, mitochondrial dysfunction, oxidative stress, neuroinflammation, genetic susceptibility, and abnormal protein aggregation contribute to disease progression²⁰.

The loss of dopaminergic neurons results in motor symptoms including bradykinesia, resting tremor, rigidity, and postural instability, together with non-motor manifestations such as cognitive impairment, depression, autonomic dysfunction, and sleep disturbances. Current research focuses on identifying molecular mechanisms, genetic factors, and biomarkers for early diagnosis and therapeutic intervention²¹.

Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder characterized by degeneration of upper and lower motor neurons, leading to muscle weakness, atrophy, paralysis, and respiratory failure. Although relatively rare, ALS is associated with rapid disease progression and poor prognosis²².

Early diagnosis remains difficult because the initial symptoms often resemble other neuromuscular disorders. Clinical manifestations may also include cognitive and behavioral impairment, particularly in patients with frontotemporal involvement. Advances in genetic research and diagnostic criteria have improved the understanding of disease heterogeneity and facilitated earlier diagnosis²³.

Diagnosis is primarily based on clinical history, neurological examination, electrophysiological studies, and genetic testing where appropriate. Despite these advances, diagnosis is frequently delayed because of the lack of reliable biomarkers and overlapping clinical features²⁴. Recent developments in biofluid biomarkers, neuroimaging, and electrophysiological techniques have improved disease characterization. Familial ALS demonstrates considerable genotype–phenotype variability, and some patients exhibit multisystem involvement, including frontotemporal dementia^{25,26}.

Huntington's Disease

Huntington's disease (HD) is an inherited neurodegenerative disorder caused by expansion of CAG trinucleotide repeats in the *HTT* gene. It is characterized by progressive motor dysfunction, cognitive decline, and psychiatric disturbances²⁷.

Clinical manifestations usually begin during adulthood and include chorea, impaired coordination, behavioral abnormalities, and cognitive impairment. Psychiatric symptoms frequently precede motor dysfunction. Progressive degeneration of neurons within the basal ganglia results in worsening neurological disability and loss of functional independence^{28,29,30}.

Multiple Sclerosis

Multiple sclerosis (MS) is a chronic immune-mediated demyelinating disease of the central nervous system characterized by inflammation, demyelination, and axonal degeneration. Immune-mediated destruction of the myelin sheath disrupts neuronal signal transmission, resulting in neurological dysfunction³¹.

Clinical manifestations include visual disturbances, muscle weakness, numbness, impaired coordination, gait abnormalities, fatigue, and cognitive dysfunction. MS is classified into relapsing-remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS), clinically isolated syndrome (CIS), and radiologically isolated syndrome (RIS) based on disease progression and clinical presentation as shown in figure 2.



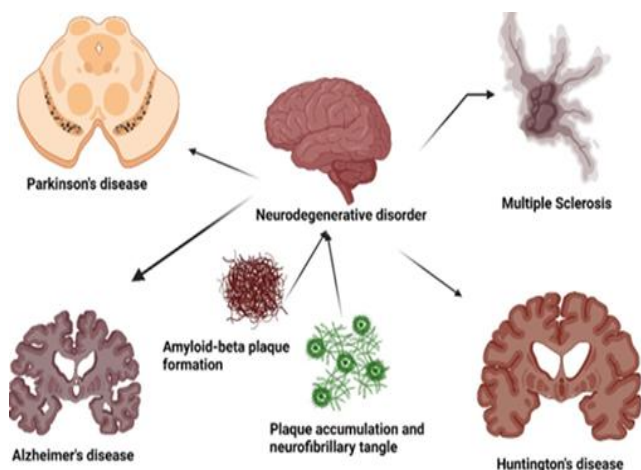


Figure 2: Illustration of various neurodegenerative disorders such as Parkinson's disease, Multiple sclerosis, Alzheimer's disease, and Huntington's disease.

Drug Delivery Challenges

The blood–brain barrier (BBB) is a highly selective physiological barrier that regulates the transport of substances between the bloodstream and the central nervous system (CNS), thereby maintaining neural homeostasis. Although the BBB plays an essential role in protecting the brain, it also represents a major obstacle to the treatment of neurodegenerative diseases, neuroinfections, and brain tumors by limiting drug penetration into the CNS. Most conventional therapeutic agents have poor BBB permeability because of their high molecular weight and low lipid solubility, resulting in reduced therapeutic efficacy³².

Drug delivery to the brain requires the integration of pharmaceutical, biological, and engineering approaches. In addition to the BBB, the blood–cerebrospinal fluid barrier (BCSFB) also regulates the movement of molecules into the CNS, protecting neurons from toxins, pathogens, endocrine fluctuations, and metabolic waste. However, these protective barriers restrict the entry of many therapeutic agents, highlighting the need for innovative drug delivery systems to improve CNS drug availability³³.

Several strategies have been developed to enhance drug transport across the BBB, including receptor-mediated transport, nanoparticle-based carriers, liposomes, exosomes, focused ultrasound, and chemical modification of drugs to improve their permeability. These approaches aim to increase drug bioavailability within the brain while maintaining therapeutic safety and efficacy for the management of neurodegenerative diseases³⁴.

Safety, Off-Target Effects, and Toxicity

Evaluation of on-target and off-target effects is essential for improving the safety and efficacy of therapeutic agents used in neurodegenerative diseases. Integrated molecular approaches enable comprehensive analysis of transcriptomic activity at both quantitative and qualitative levels, allowing high-resolution identification of regulatory elements, affected promoters, and genes involved in drug-

induced molecular changes. Such analyses facilitate the early detection of potential adverse effects, improve understanding of drug mechanisms, and provide valuable insights into molecular pathways associated with therapeutic responses. These approaches also assist in identifying both known and previously unrecognized off-target effects, thereby supporting the development of safer and more effective therapeutic strategies while minimizing toxicity during drug development and clinical application^{35,36}.

Clinical Translation and Current Evidence

Clinical translation remains a major challenge in the management of neurodegenerative diseases despite significant advances in experimental research. Implementation science provides a systematic framework for promoting the integration of research findings and evidence-based interventions into routine clinical practice, thereby improving the quality and effectiveness of healthcare services³⁷. The use of determinant frameworks facilitates the identification of factors that influence clinical trial outcomes and provides a structured approach for adapting interventions to different healthcare settings while improving implementation strategies. During the evaluation process, qualitative research methods such as focus group discussions and key informant interviews are commonly employed to understand stakeholder perspectives, identify implementation barriers, and optimize the successful translation of research findings into clinical practice^{38,39}.

Preclinical and Clinical Trial Data

Neurodegenerative diseases affect a substantial proportion of the ageing population and continue to represent an important global public health challenge. In addition to ageing, disease development and progression are influenced by several genetic, environmental, biological, psychological, nutritional, and lifestyle factors^{40,41}. The development of reliable experimental models remains essential for improving the understanding of disease mechanisms and evaluating potential therapeutic interventions before clinical application. However, the complexity of neurodegenerative disorders and the limited availability of representative disease models have contributed to the slow progress of neurological drug development^{42,43}. Therefore, preclinical studies should validate experimental models that closely mimic human disease pathology before their translation into clinical trials. Continued research focusing on improved disease models, neuroprotective compounds, antioxidant therapies, and innovative treatment approaches is expected to accelerate therapeutic development and improve clinical outcomes in patients with neurodegenerative diseases⁴⁴.

Non-Coding RNAs as Diagnostic and Prognostic Biomarkers

Biomarkers are measurable biological molecules that reflect physiological processes, pathological conditions, or responses to therapeutic interventions. They play a critical role in early disease detection, diagnosis, prognosis, disease monitoring, and evaluation of treatment response⁴⁵. In

recent years, increasing attention has been directed toward non-coding RNAs (ncRNAs), including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), circular RNAs (circRNAs), and PIWI-interacting RNAs (piRNAs), because of their important regulatory functions and disease-specific expression profiles. Altered expression of these ncRNAs has been associated with several pathological conditions, including neurodegenerative diseases, cancer, cardiovascular disorders, and autoimmune diseases, supporting their potential as diagnostic and prognostic biomarkers⁴⁶.

In addition to their diagnostic value, ncRNAs regulate numerous biological processes, including cell proliferation, differentiation, apoptosis, inflammation, and neuronal function. Dysregulation of ncRNA expression contributes to disease pathogenesis by modulating multiple molecular pathways and may act as either upstream regulators or downstream effectors of disease progression. Furthermore, circulating ncRNAs detected in biological fluids provide a minimally invasive approach for disease diagnosis, prognosis, and monitoring of therapeutic responses through liquid biopsy. Although biological variability initially limited their clinical application, advances in sequencing technologies, analytical methods, and bioinformatics have significantly improved their reproducibility and accelerated their translation into clinical practice^{47,48}.

Regulatory and Ethical Considerations

Successful clinical implementation of ncRNA-based diagnostics and artificial intelligence (AI)-assisted technologies requires strict adherence to established regulatory and ethical standards. Regulations such as the General Data Protection Regulation (GDPR) ensure the protection of patient privacy through informed consent, data minimization, pseudonymization, and transparent handling of clinical information, particularly during long-term monitoring of patients with neurodegenerative diseases. In addition, the Medical Device Regulation (EU 2017/745) governs AI-based diagnostic software and clinical decision-support systems by requiring comprehensive clinical validation, safety assessment, traceability, and regulatory compliance before their integration into healthcare practice. Ethical principles including patient autonomy, transparency, fairness, prevention of harm, and equitable healthcare delivery should guide the development and implementation of these technologies. Active participation of patients and caregivers, together with strategies to minimize algorithmic bias and improve interpretability, is essential for ensuring trust, safety, and responsible clinical adoption⁴⁹.

Role of Clinical Pharmacists

Clinical pharmacists play an important role in optimizing pharmacotherapy for patients with neurodegenerative diseases through individualized medication management based on disease stage, patient characteristics, and associated comorbidities. They contribute to the prevention of drug–drug interactions associated with polypharmacy,

recommend dosage adjustments according to renal and hepatic function, and continuously monitor treatment safety and therapeutic effectiveness.

In addition, clinical pharmacists improve medication adherence by providing patient counselling, simplifying medication regimens, and promoting the use of adherence-support tools such as pill organizers and reminder systems, particularly in patients with cognitive impairment. Close collaboration with neurologists, psychiatrists, nurses, social workers, and other healthcare professionals further strengthens multidisciplinary patient care and supports clinical research aimed at developing disease-modifying and neuroprotective therapeutic strategies⁵⁰.

Challenges and Limitations

Neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis, continue to present major diagnostic and therapeutic challenges worldwide. Early diagnosis remains difficult because of limited disease-specific biomarkers, heterogeneous clinical manifestations, and the limitations of current diagnostic methods despite significant advances in understanding disease pathogenesis. Therapeutic development is further complicated by the blood–brain barrier, challenges associated with effective drug delivery, and the limited availability of disease-modifying therapies. In addition, restricted access to specialized healthcare services, caregiver burden, inadequate healthcare resources, and financial constraints continue to adversely affect disease management and patient outcomes. Continued research, innovation, and multidisciplinary collaboration are therefore essential for improving diagnostic accuracy and developing more effective therapeutic strategies for neurodegenerative diseases⁵¹.

Future Perspectives

Future therapeutic strategies should focus on regulating neuroinflammation, modulating microglial activation, and promoting neuroprotection through both pharmacological and non-pharmacological interventions. Lifestyle modifications, including balanced nutrition, regular physical activity, and cognitive training, have demonstrated the potential to delay disease onset and slow disease progression. Emerging therapeutic approaches, including gene-editing technologies, stem cell therapy, immunotherapy targeting misfolded proteins, and RNA-based therapeutics such as antisense oligonucleotides (ASOs), have shown encouraging results and represent promising strategies for the management of neurodegenerative diseases.

CONCLUSION

The global burden of neurodegenerative diseases continues to increase because of population ageing and increased life expectancy, emphasizing the urgent need for effective preventive and therapeutic strategies. Addressing modifiable risk factors, improving early diagnosis, and developing disease-modifying therapies remain major



priorities in clinical research. Neurodegenerative diseases also exhibit considerable variation across age, sex, and socioeconomic groups, highlighting the importance of personalized healthcare strategies and equitable resource allocation. Recent advances in understanding intracellular signalling pathways and molecular mechanisms have facilitated the identification of novel therapeutic targets and improved insight into disease pathogenesis. Future research should focus on translating these discoveries into effective clinical interventions while exploring both pharmacological and non-pharmacological approaches for the prevention and management of neurodegenerative diseases.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- Choonara YE, Pillay V, Du Toit LC, Modi G, Naidoo D, Ndesendo VMK, Sibambo SR. Trends in the molecular pathogenesis and clinical therapeutics of common neurodegenerative disorders. 2009;10:2510-2557. *Int J Mol Sci*. doi:10.3390/IJMS10062510.
- Clarke CE. Medical management of Parkinson's disease. *Pharm Ther*. 2008;33:590. doi:10.1136/jnnp.72.suppl_1.i22.
- Huang Y, Li Y, Pan H, Han L. Global, regional, and national burden of neurological disorders in 204 countries and territories worldwide. *J Glob Health*. 2023;13:04160. doi:10.7189/JOGH.13.04160.
- Jiménez-Balado J, Eich TS. GABAergic dysfunction, neural network hyperactivity and memory impairments in human aging and Alzheimer's disease. *Semin Cell Dev Biol*. 2021;116:146-159. doi:10.1016/j.semc.2021.01.005.
- Natasha FM, Catherine D, John K, et al. The experience of Parkinson's disease in Hai district, Tanzania. *J Neurodegener Disord*. 2021;4(1):122-128. doi:10.36959/459/606.
- Natasha FM, Catherine D, John K, et al. The experience of Parkinson's disease in Hai district, Tanzania. *J Neurodegener Disord*. 2021;4(1):122-128. doi:10.36959/459/606.
- Lee RC, Feinbaum RL, Ambros V. The *C. elegans* heterochronic gene *lin-4* encodes small RNAs with antisense complementarity to *lin-14*. *Cell*. 1993;75:843-854. doi:10.1016/0092-8674(93)90529-Y. PMID:8252621.
- Ha M, Kim VN. Regulation of microRNA biogenesis. *Nat Rev Mol Cell Biol*. 2014;15:509-524. doi:10.1038/nrm3838. PMID:25027649.
- Ender C, Meister G. Argonaute proteins at a glance. *J Cell Sci*. 2010;123:1819-1823.
- Ender C, Meister G. Argonaute proteins at a glance. *J Cell Sci*. 2010;123:1819-1823.
- Sanger HL, Klotz G, Riesner D, Gross HJ, Kleinschmidt AK. Viroids are single-stranded covalently closed circular RNA molecules existing as highly base-paired rod-like structures. *Proc Natl Acad Sci U S A*. 1976;73(11):3852-3856. doi:10.1073/pnas.73.11.3852. PMID:1069269.
- Ye CY, Chen L, Liu C, Zhu QH, Fan L. Widespread noncoding circular RNAs in plants. *New Phytol*. 2015;208(1):88-95. doi:10.1111/nph.13585. PMID:26204923.
- McEwen BS. Neurobiological and systemic effects of chronic stress. *Chronic Stress*. 2017;1. doi:10.1177/2470547017692328.
- Ajmal MR. Protein misfolding and aggregation in proteinopathies: causes, mechanism and cellular response. *Diseases*. 2023;11:30. doi:10.3390/diseases11010030.
- Koszła O, Sołek P. Misfolding and aggregation in neurodegenerative diseases: protein quality control machinery as potential therapeutic clearance pathways. *Cell Commun Signal*. 2024;22(1). doi:10.1186/s12964-024-01791-8.
- Koszła O, Sołek P. Misfolding and aggregation in neurodegenerative diseases: protein quality control machinery as potential therapeutic clearance pathways. *Cell Commun Signal*. 2024;22(1). doi:10.1186/s12964-024-01791-8.
- Lamprey RNL, Chaulagain B, Trivedi R, Gothwal A, Layek B, Singh J. A review of the common neurodegenerative disorders: current therapeutic approaches and the potential role of nanotherapeutics. *Int J Mol Sci*. 2022;23. doi:10.3390/ijms23031851.
- Breijyeh Z, Karaman R. Comprehensive review on Alzheimer's disease: causes and treatment. *Molecules*. 2020;25. doi:10.3390/molecules25245789.
- Breijyeh Z, Karaman R. Comprehensive review on Alzheimer's disease: causes and treatment. *Molecules*. 2020;25. doi:10.3390/molecules25245789.
- Oxid Med Cell Longev. 2015;Article 352723. doi:10.1155/2015/352723.
- Epigenetic modification in Parkinson's disease. *Front Cell Dev Biol*. 2023;11:1123621. doi:10.3389/fcell.2023.1123621.
- Stem cell therapy for Parkinson's disease. *Adv Exp Med Biol*. 2020;1266:21-38. doi:10.1007/978-981-15-4370-8_3.
- Ryan M, Heverin M, McLaughlin RL, Hardiman O. Lifetime risk and heritability of amyotrophic lateral sclerosis. *JAMA Neurol*. 2019;76:1367-1374.
- Goutman SA, Hardiman O, Al-Chalabi A, Chió A, Savelieff MG, Kiernan MC, Feldman EL. Recent advances in the diagnosis and prognosis of amyotrophic lateral sclerosis. *Lancet Neurol*. 2022;21:480-493.
- Mathis S, Goizet C, Soulages A, Vallat JM, Masson GL. Genetics of amyotrophic lateral sclerosis: a review. *J Neurol Sci*. 2019;399:217-226. doi:10.1016/j.jns.2019.02.030.
- Parobkova E, Matej R. Amyotrophic lateral sclerosis and frontotemporal lobar degenerations: similarities in genetic background. *Diagnostics*. 2021;11:509. doi:10.3390/diagnostics11030509. PMID:33805659.
- Illarioshkin SN, Klyushnikov SA, Vigont VA, Seliverstov YA, Kaznacheyeva EV. Molecular pathogenesis in Huntington's disease. *Biochemistry (Moscow)*. 2018;83(9):1030-1039. doi:10.1134/S0006297918090043. PMID:30472941.



28. Mayo Clinic. Huntington's disease – symptoms and causes. Mayo Clinic. Retrieved April 25, 2025.
29. Sudhakar V, Richardson RM. Gene therapy for neurodegenerative diseases. *Neurotherapeutics*. 2019;16(1):166-175. doi:10.1007/s13311-018-00694-0. PMID:30542906.
30. Reiner A, Dragatsis I, Dietrich P. Genetics and neuropathology of Huntington's disease. In: *Pathophysiology, Pharmacology, and Biochemistry of Dyskinesia. International Review of Neurobiology*. Vol. 98. 2011. p.325-372. doi:10.1016/B978-0-12-381328-2.00014-6. ISBN:978-0-12-381328-2.
31. Singh R, Lillard JW. Nanoparticle-based targeted drug delivery. *Exp Mol Pathol*. 2009;86(3):215-223. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3249419/>
32. Orime K, et al. Lipid-lowering agents inhibit hepatic steatosis in a non-alcoholic steatohepatitis-derived hepatocellular carcinoma mouse model. *Eur J Pharmacol*. 2016;772:22-32.
33. Huang Y, Furuno M, Arakawa T, Takizawa S, de Hoon M, Suzuki H, et al. A framework for identification of on- and off-target transcriptional responses to drug treatment. *Sci Rep*. 2019;9(1):17603. Available from: <https://www.nature.com/articles/s41598-019-54180-4>
34. Eccles MP, Mittman BS. Welcome to implementation science. *Implement Sci*. 2006;1(1):1.
35. Nilsen P, Bernhardtsson S. Context matters in implementation science: a scoping review of determinant frameworks that describe contextual determinants of implementation outcomes. *BMC Health Serv Res*. 2019;19(1):189-96.
36. Hamilton AB, Finley EP. Qualitative methods in implementation research: an introduction. *Psychiatry Res*. 2019;280:112516.
37. Gammon K. Neurodegenerative disease: brain windfall. *Nature*. 2014;515:299-300. doi:10.1038/nj7526-299a.
38. Domínguez LJ, Barbagallo M. Nutritional prevention of cognitive decline and dementia. *Acta Biomed*. 2018;89:276-290. doi:10.23750/abm.v89i2.7401.
39. Calabrese M, Gajofatto A, Gobbin F, Turri G, Richelli S, Matinella A, et al. Late-onset multiple sclerosis presenting with cognitive dysfunction and severe cortical/infratentorial atrophy. *Mult Scler J*. 2015;21:580-589. doi:10.1177/1352458514542363.
40. Newman DJ, Cragg GM. Natural products as sources of new drugs over the 30 years from 1981 to 2010. *J Nat Prod*. 2012;75:311-335. doi:10.1021/np200906s.
41. *Front Behav Neurosci*. 2023 Jun 7;17. doi:10.3389/fnbeh.2023.1176777.
42. Califf RM. Biomarker definitions and their applications. *Exp Biol Med* (Maywood). 2018;243:213-221. doi:10.1177/1535370217750088. PMID:29405771.
43. Poliseno L, Lanza M, Pandolfi PP. Coding, or non-coding, that is the question. *Cell Res*. 2024;34:609-629. doi:10.1038/s41422-024-00975-8. PMID:39054345.
44. Eldakhakhny B, Sutaih AM, Siddiqui MA, Aqeeli YM, Awan AZ, Alsayegh MY, Elsamanoudy SA, Elsamanoudy A. Exploring the role of noncoding RNAs in cancer diagnosis, prognosis, and precision medicine. *Noncoding RNA Res*. 2024;9:1315-1323. doi:10.1016/j.ncrna.2024.06.015. PMID:39764154.
45. Toden S, Goel A. Non-coding RNAs as liquid biopsy biomarkers in cancer. *Br J Cancer*. 2022;126:351-360. doi:10.1038/s41416-021-01672-8. PMID:35013579.
46. ResearchGate. ncRNAs as diagnosis and prognostic biomarkers in LC [Internet]. Available from: https://www.researchgate.net/figure/ncRNAs-as-diagnosis-and-prognostic-biomarkers-in-LC-ncRNAs-noncoding-RNAs_fig5_365146361
47. Department of Experimental and Clinical Biomedical Sciences, University of Florence, Viale Morgagni 50, 50134 Florence, Italy. Authors to whom correspondence should be addressed.
48. Trideva Sastri Koduru, Osmani AM, Singh E, Dutta S. *The Neurodegeneration Revolution*. Academic Press; 2024.
49. Challenges and opportunities in neurodegenerative diseases management – ScienceDirect.
50. Department of Pharmacy Practice, JSS College of Pharmacy, JSS Academy of Higher Education & Research, Mysuru, India.
51. Fereshtehnejad SM, Vosoughi K, Heydarpour P, Sepanlou SG, Farzadfar F, Tehrani-Banihashemi A, et al. Burden of neurodegenerative diseases in the Eastern Mediterranean Region, 1990–2016: findings from the Global Burden of Disease Study 2016. *Eur J Neurol*. 2019;26(10):1252-1265.

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