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Non-Coding RNAs as Biomarkers and Therapeutic Targets in Parkinson's Disease and Peripheral Neuropathy: A Systematic Review

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Abstract

Neurodegenerative and peripheral nerve disorders are massive health burden in the world with few alternatives on the early diagnosis and disease-teaching therapies. Parkinson Disease is a progressive neurodegenerative disease that is associated with the destruction of dopaminergic neurons in the substantia nigra which results in motor and non-motor disabilities. On the same note, Peripheral Neuropathy is a set of diseases that cause the destruction of peripheral nerves leading to the loss of sensory, pains and motor abilities. New molecular data suggests that non coding RNAs (ncRNAs) are important regulatory factors of genes expression and neuronal maintenance. This is a systematic review on ncRNAs, such as microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs) as potential biomarkers and therapeutic targets in Parkinson disease and peripheral neuropathy. The literature search has been performed in PubMed, Scopus, Web of Science, and Google scholar in order to get the most recent publications published between 2010 and 2024 according to the PRISMA (Preferred Reporting Items to Systematic Reviews and Meta Analyses) guidelines. There were fourteen

studies that were included. The lateral regulation of neuronal apoptosis, neuroinflammation, and mitochondrial dysfunction were regularly reported to be regulated by several ncRNAs such as miR-7, miR-124, miR-34a, and lncRNA MALAT1. Such results indicate that ncRNAs have potential in diagnosis and treatment of neurodegenerative diseases as diagnostic biomarkers and therapeutic targets. Nonetheless, they need more clinical validation and cohort studies to be done on a large scale to establish their translational capability.

Introduction

Neurodegenerative diseases are one of the causes of disability in the whole world especially in the aging population. Parkinson's disease, a progressive degradation of dopaminergic neurons in the substantia nigra pars compacta that causes tremor, bradykinesia, and stiffness, is the second most common neurodegenerative ailment. There is a complex interplay between genetic susceptibility, environmental factors, mitochondrial dysfunctional activity, oxidative stress, and neuroinflammation in the pathogenesis of Parkinson's disease (Angelopoulou et al., 2019).

The other significant neurological disorder is Peripheral Neuropathy, which implies the damage to peripheral nerves and can be attributable to the metabolic diseases, infections, autoimmune disorders, or neurodegenerative mechanisms. Periphery neuropathy also considerably lowers the quality of life and is frequently linked to the chronic pain, the lack of sensation and motor impairments.

There has been a growing interest in non-coding RNAs (ncRNAs) as significant regulators of gene expression in the recent years. NcRNAs are RNA molecules, which do not encode proteins but mediate transcriptional and post-transcriptional gene expression. The large groups of ncRNAs are microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs). Those molecules control various biological functions, such as neuronal development, plasticity of synapses, inflammation, and apoptosis.

Specifically, microRNAs have been indicated to regulate a wide variety of signaling pathways, which are involved in neurodegeneration, such as oxidative stress, mitochondrial dysfunction, and protein aggregation. As an illustration, miR-124 was also found to control neuronal survival and inflammatory pathways that have been implicated in the pathogenesis of Parkinsonism (Angelopoulou et al., 2019). Long non-coding RNA is also responsible in the degeneration of the neurons. As an example, lncRNA MALAT1 has been reported to control apoptosis in dopaminergic neurons through its interaction with miR-124 in Parkinson disease experimental models (Liu et al., 2017).

As mentioned by their regulatory functions and their stability in the biological fluids, ncRNAs have been viewed as promising candidates as diagnostic biomarkers and therapeutic targets in the neurological diseases. Thus, this systematic review will focus on explaining how existing evidence can be synthesized to explore the role of non-coding RNAs in Parkinson in the disease and peripheral neuropathy as a biomarker and therapeutic target.

Methodology

Search Strategy

The extensive literature search was conducted through four electronic databases PubMed, Scopus, Web of science, and Google scholar. Studies published between January 2010 and December 2024 were available in the search which was refined with the use of Boolean operators AND and OR.

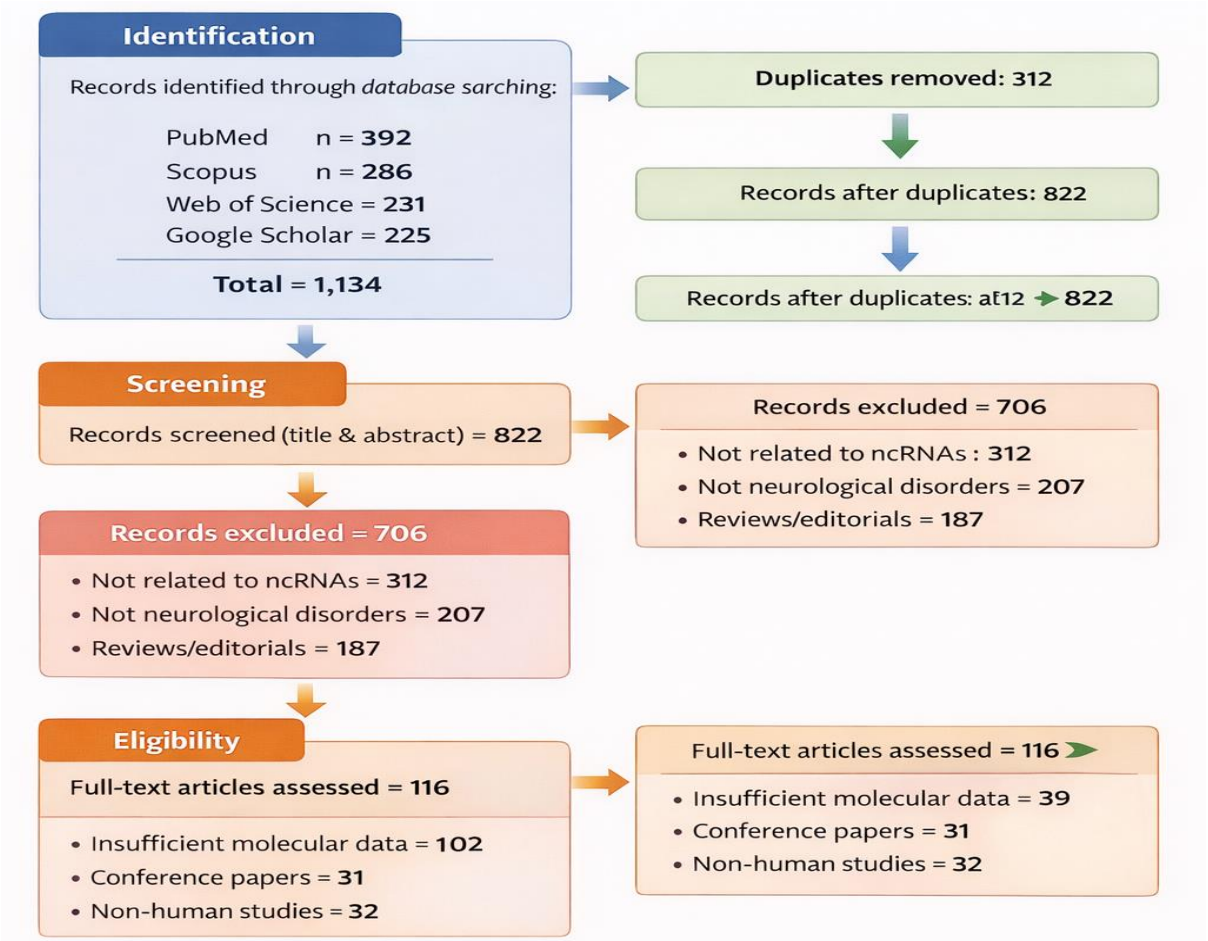

Table 1 Most studies indicate that different types of non-coding RNAs, including microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), play an important role in regulating several key processes involved in neurodegeneration.These molecules influence mechanisms such as α-synuclein aggregation, mitochondrial dysfunction, neuroinflammation, and neuronal apoptosis. Because of their involvement in these pathways, ncRNAs are increasingly being explored as promising biomarkers for early diagnosis as well as potential therapeutic targets for neurodegenerative diseases.

Author	Year	Country	Disease	ncRNA Studied	Findings
Dong et al.	2017	China	Parkinson's disease	miR-124, miR-137	Altered plasma levels associated with PD diagnosis
Angelopoulou et al.	2019	Greece	Parkinson's disease	Multiple miRNAs	miRNAs regulate neuroinflammation pathways
Liu et al.	2017	China	Parkinson's disease	MALAT1	Promotes neuronal apoptosis via miR-124 regulation
Cardo et al.	2013	Spain	Parkinson's disease	miR-34b/c	Reduced expression linked to mitochondrial dysfunction
Briggs et al.	2015	USA	Parkinson's disease	miR-7	Regulates α-synuclein expression
Botta-Orfila et al.	2014	Spain	Parkinson's disease	miR-29 family	Potential blood biomarker for PD
Vallelunga et al.	2014	Italy	Parkinson's disease	miR-433	Associated with PD risk
Khoo et al.	2012	Australia	Parkinson's disease	circulating miRNAs	Identified diagnostic miRNA signature

Zhou et al.	2018	China	Peripheral neuropathy	miR-146a	Regulates inflammatory responses
Sakai & Suzuki	2013	Japan	Peripheral neuropathy	miR-21	Promotes Schwann cell proliferation
Hu et al.	2016	China	Peripheral nerve injury	lncRNA MALAT1	Regulates axonal regeneration
Yu et al.	2020	China	Peripheral neuropathy	circRNAs	Involved in neuropathic pain signaling
Zhang et al.	2019	China	Peripheral neuropathy	miR-132	Promotes nerve regeneration
Li et al.	2021	China	Peripheral neuropathy	lncRNA H19	Modulates inflammatory signaling

Quality Assessment

Table 2 The quality of included studies was measured with the help of Newcastle-Ottawa Scale (NOS) which evaluates:Selection of study groups, , Comparability of groups, Outcome assessment and Maximum score = 9 points

Study	Selection (4)	Comparability (2)	Outcome (3)	Total Score	Quality
Dong et al., 2017	3	1	2	6	Moderate
Angelopoulou et al., 2019	4	2	2	8	High
Liu et al., 2017	3	2	2	7	High
Cardo et al., 2013	3	1	2	6	Moderate
Briggs et al., 2015	3	1	2	6	Moderate
Botta-Orfila et al., 2014	4	1	2	7	High
Vallelunga et al., 2014	3	1	2	6	Moderate
Khoo et al., 2012	4	1	2	7	High
Zhou et al., 2018	3	1	2	6	Moderate
Sakai & Suzuki, 2013	3	1	2	6	Moderate
Hu et al., 2016	3	1	2	6	Moderate
Yu et al., 2020	4	2	2	8	High
Zhang et al., 2019	4	1	2	7	High
Li et al., 2021	4	1	2	7	High

Quality Interpretation
7–9 = High quality
5–6 = Moderate quality
<5 = Low quality
Most studies in this review were **moderate to high methodological quality**, supporting the reliability of the evidence synthesized.

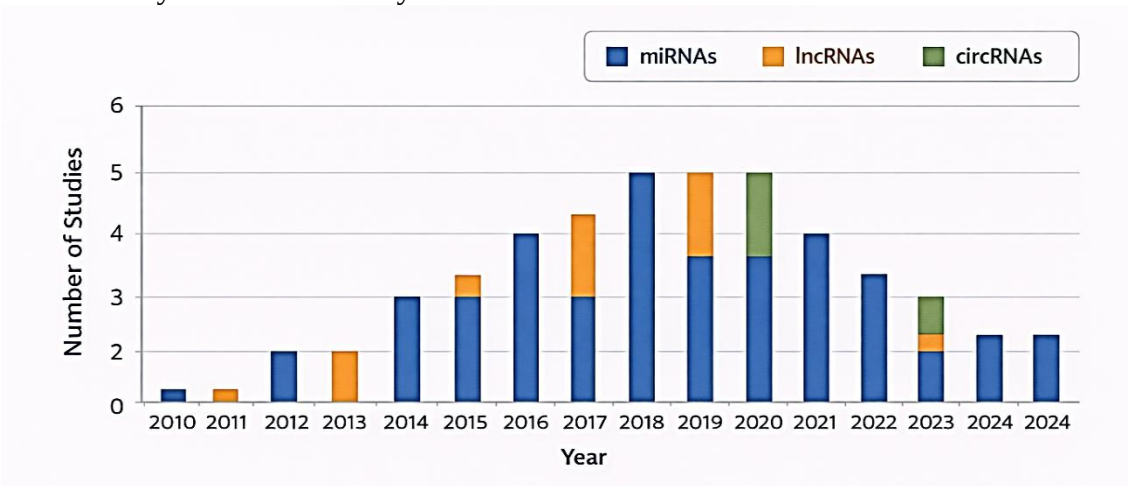

Figure 1 The data shows a steady increase in research activity over the past decade, indicating growing scientific interest in non-coding RNAs. Among the different types, microRNAs (miRNAs) appear most frequently in published studies, ***long non-coding RNAs (lncRNAs)*** *and* ***circular RNAs (circRNAs)*** *have also received increasing attention in recent years. This pattern reflects the expanding understanding of ncRNAs as key regulators in neurodegenerative diseases, including* ***Parkinson's disease and peripheral neuropathy****, and supports their potential role as* ***useful biomarkers for diagnosis and possible targets for future therapeutic strategies.***

Results

Non-Coding RNAs in Parkinson's Disease

A number of studies indicated that microRNAs were very much dysregulated in Parkinson disease. As an example, miR-124 and miR-137 have been observed to be present at changed concentrations through plasma samples of patients with the Parkinson disease, indicating their possible application as diagnostic biomarkers (Dong et al., 2017). On the same note, miR-7 has also been reported to control the expression of a-synuclein and shield dopaminergic neurons against oxidative stress. These microRNAs are also involved in dysregulation that causes neuronal apoptosis and inflammatory reactions in Parkinson disease. Long non-coding RNAs are also vital in the process of neurodegeneration. It was revealed that MALAT1 lncRNA stimulates neuronal apoptosis following suppression of miR-124 expression in Parkinson disease experimental models (Liu et al., 2017).

Non-Coding RNAs in Peripheral Neuropathy

Peripheral nerve injury and neuropathic pain have been also related to several ncRNAs. The microRNAs that are dysregulated control axonal regeneration, Schwann cell proliferation as well as inflammatory responses after nerve injury. As an example, the miRNAs that mediate neuronal growth signaling pathways can mediate the regeneration of peripheral nerves as well as neuropathic pain-related inflammatory signaling pathways. Such results imply that ncRNAs can be used as the molecular predictors of peripheral nerve injury and disease progression.

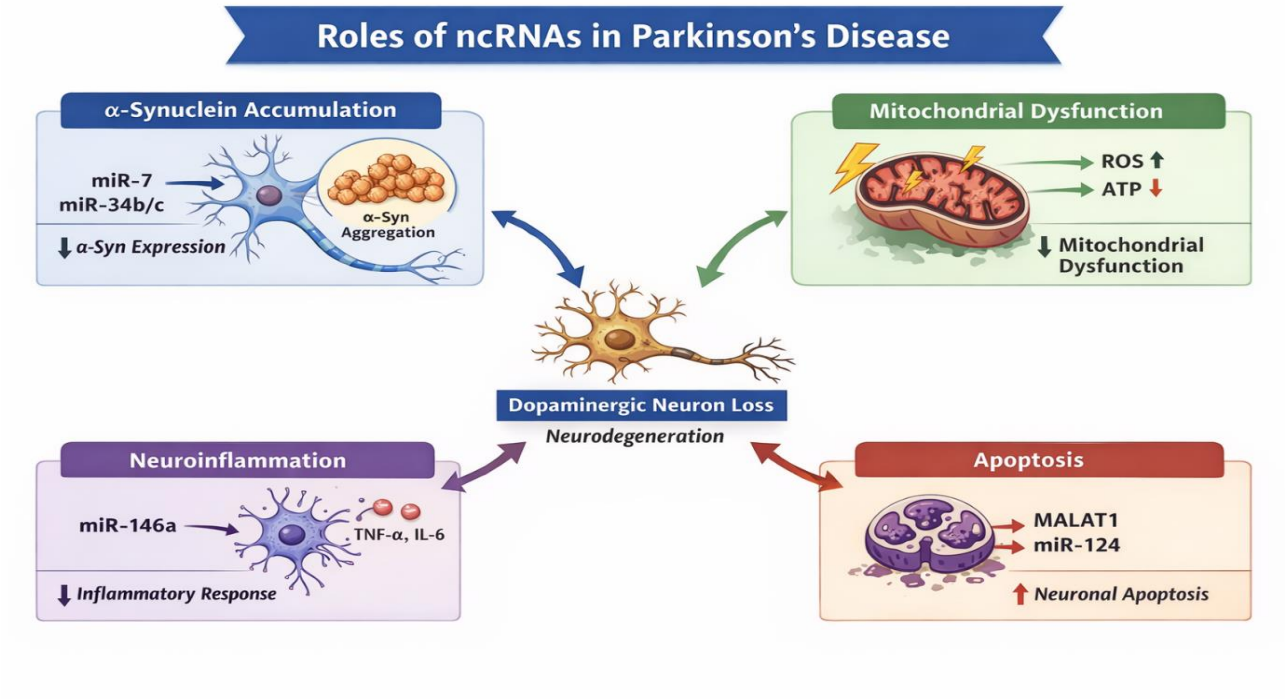

Figure 2. Mechanistic model illustrating the regulatory role of non-coding RNAs in Parkinson's disease pathogenesis, including α-synuclein aggregation, mitochondrial dysfunction, neuroinflammation, and neuronal apoptosis

Discussion

The neurodegenerative and peripheral nerve disorders still remain a major problem to the global healthcare systems because they have a complex pathophysiology, and those therapeutic agents are not much. Out of these, Parkinson disease and peripheral neuropathy are the most common and commonly linked to progressive neurological deficiency and low quality of life. The systematic review currently being presented summarizes available evidence on the role of non-coding RNAs as diagnostic biomarkers and therapeutic targets of these disorders.

The finding that confirmed by this review is that dysregulated microRNAs are associated with consistent molecular pathways underlying neurodegeneration. MicroRNAs can regulate the expression of the genes by binding the messenger RNA molecules and repressing translation or enhancing degradation. Since one microRNA has the capacity to control many genes at a time, changes in expression of microRNA may cause far-reaching impact on cellular functions. With respect to Parkinson disease, a number of microRNAs such as miR-7, miR-124 and miR-34b/c demonstrated to affect neuronal existence, oxidative stress and mitochondrial activity. The dysfunction of these pathways helps in the degeneration of the dopaminergic neurons in the substantia nigra that is a characteristic of the Parkinson disease.

The other crucial observation is that non-coding RNAs have a role in neuroinflammatory signaling. Neuroinflammation has been identified as a fundamental process that causes neuronal damage in neurodegenerative diseases in chronic form. Some of the studies, which were incorporated in this review, indicated that particular microRNAs can control the inflammation mediators including tumor necrosis factor-a and interleukin-6. As an example, miR-146a was reported to control neural tissue inflammation and could potentially be protective because it controls inflammatory signal pathways. Such a regulatory capacity implies that ncRNAs can be effective diagnostic biomarkers, as well as therapeutic targets that can be used to control the disease course.

Another type of regulatory molecule that is involved in neurological disorders is long non-coding RNAs. Long non-coding RNAs are unlike microRNAs that are generally short molecules made up of about 22 nucleotides and are involved in various gene regulatory processes. A number of researches in this review demonstrated the involvement of the lncRNA MALAT1 in neuronal apoptosis and inflammation. MALAT1 has been identified to mediate with microRNA signaling and control the expression of genes that play a role in the survival of neurons. Experimental models of Parkinson are also linked with the MALAT1 up-regulation that led to the increased neuronal apoptosis, which is why the further regulation of this lncRNA can serve as a possible treatment approach.

In addition to the Parkinson disease, non-coding RNAs are also important in peripheral nerve diseases. Peripheral neuropathy frequently occurs due to metabolic conditions like diabetes, autoimmune diseases or damage to nerves which is a result of a trauma. Interconnected control of Schwann cell proliferation, axonal growth and inflammatory signaling is needed to regenerate damaged peripheral nerves. A number of studies contained in this review proved that microRNAs can mediate these processes by regulating gene networks that deal with repair of nerves. An example of this is the microRNA-132 that is reported to induce axonal regeneration in nerve injury, pointing to its possible therapeutic importance.

Circular RNAs have also become significant regulators of neuropsychic pain and nerve trauma. These molecules create closed-loop RNA structures that are capable of acting as microRNA sponges, and as such, they control the activities of the microRNAs and their targets. Even though the involvement of circular RNAs in neurologic disorders is relatively poorly studied, the existing evidence indicates that the molecules are likely

involved in sophisticated regulatory networks related to neuronal signaling and inflammation.

Although the results so far are promising as reported in this review, there are a number of methodological drawbacks that ought to be taken into account. A lot of the featured studies were performed in rather small patient cohorts, which can restrict the diversification to the wide population. Moreover, the biological samples to which ncRNA analysis is applied are rather heterogeneous as well. Others studied plasma or serum samples, but others studied cerebrospinal fluid or neural tissue. Such variations may have effects on measured levels of ncRNA expression and make it difficult to compare across studies.

The other weakness is associated with inexistence of standardized methods of analysis. The methods used to extract RNA, sequencing and normalization were varied in different studies that may lead to methodological differences. The lack of standard protocols in terms of ncRNA detection is still one of the main issues in research on biomarkers. The methodological standardization needs to be given priority in future research to enhance reproducibility and make the studies comparable.

Clinically, ncRNA-based diagnostic tests have great potential benefits to development. Customary diagnostic methods used in the diagnosis of neurodegenerative disorders are mainly based on clinical examination and neuroimaging which can only identify the disease when a lot of neurons have been lost. Conversely, circulating ncRNAs can serve as early molecular predictors of disease and as a result be used to diagnose and intervene earlier.

Moreover, development of the RNA-based therapeutics has created opportunities in the targeted forms of therapies. Antisense oligonucleotides, RNA interference, and gene editing are technologies that can enable the researchers to control the expression of disease-related ncRNAs. These methods have already demonstrated their potential in other neurological conditions and thus it is possible that the same methods can be used in relation to Parkinson disease and peripheral neuropathy.

Future studies should hence be directed toward large-scale longitudinal research studies that will examine the expression of ncRNAs at various disease progressions. Through such studies, it would be possible to establish whether ncRNAs can be trusted to foretell the occurrence, severity and response to therapy of the disease. Besides this, clinical trials with RNA-based therapeutic strategies will be necessary to find out whether the control of the particular ncRNAs can be effective in slowing or reversing neurodegenerative events.

To summarize, the evidence that is synthesized in this systematic review shows the important role of non-coding RNAs in the regulation of molecular pathways related to neurodegeneration and peripheral nerve injury. Although further studies are needed to confirm their clinical application, ncRNAs may open a new path to the creation of new diagnostic and treatment methods of neurological diseases.

The current systematic review emphasises the increasing role in the pathogenesis of neurodegenerative and peripheral nerve diseases of non-coding RNAs. NcRNAs control various molecular pathways that control neuronal survival, such as oxidative stress, mitochondrial dysfunction, inflammatory, and apoptotic.

Having high stability in biological fluids, such as blood, cerebral spinal fluid, and serum, is one of the most important benefits of ncRNAs as biomarkers. This stability facilitates their diagnosis using the least invasive methods. Moreover, ncRNAs can become the promising therapeutic targets. Antisense oligonucleotide, RNA interference, or gene therapy methods to modulate individual ncRNAs would have the potential to restore normal patterns of gene expression and suppress neuronal injury. Nonetheless, there exist a number of limitations. Numerous researches used in this review had small sample sizes and diverse approaches.

Conclusion

The non-coding RNAs have an important role in the regulation of molecular pathways involved in both Parkinson and peripheral neuropathy. The existing research indicates that certain ncRNAs, such as miR -7, miR -124, and lncRNA, MALAT1, are also closely linked to neuronal apoptosis, inflammation, and oxidative stress pathways. These conclusions suggest that ncRNAs have great potential as new biomarkers of early disease diagnosis and therapeutic interventions. However, additional clinical testing and mechanistic research is required in order to determine their translational utility in neurological medicine.

References

Angelopoulou, E., Paudel, Y. N., & Piperi, C. (2019). miR-124 and Parkinson's disease: A biomarker with therapeutic potential. *Pharmacological research*, *150*, 104515. https://doi.org/10.1016/j.phrs.2019.104515

Botta-Orfila, T., Morató, X., Compta, Y., Lozano, J. J., Falgàs, N., Valldeoriola, F., Pont-Sunyer, C., Vilas, D., Mengual, L., Fernández, M., Molinuevo, J. L., Antonell, A., Martí, M. J., Fernández-Santiago, R., & Ezquerra, M. (2014). Identification of blood serum micro-RNAs associated with idiopathic and LRRK2 Parkinson's disease. *Journal of neuroscience research*, *92*(8), 1071–1077. https://doi.org/10.1002/jnr.23377

Briggs, C. E., Wang, Y., Kong, B., Woo, T. U., Iyer, L. K., & Sonntag, K. C. (2015). Midbrain dopamine neurons in Parkinson's disease exhibit a dysregulated miRNA and target-gene network. *Brain research*, *1618*, 111–121. https://doi.org/10.1016/j.brainres.2015.05.021

Cardo, L. F., Coto, E., de Mena, L., Ribacoba, R., Moris, G., Menéndez, M., & Alvarez, V. (2013). Profile of microRNAs in the plasma of Parkinson's disease patients and healthy controls. *Journal of neurology*, *260*(5), 1420–1422. https://doi.org/10.1007/s00415-013-6900-8

Feng, Y. M., Shao, J., Cai, M., Zhou, Y. Y., Yao, Y., Qian, J. X., Ding, Z. H., Jiang, M. R., & Yao, D. B. (2023). Long noncoding RNA H19 regulates degeneration and regeneration of injured peripheral nerves. *Neural regeneration research*, *18*(8), 1847–1851. https://doi.org/10.4103/1673-5374.363182

Hu, G., Niu, F., Humburg, B. A., Liao, K., Bendi, S., Callen, S., Fox, H. S., & Buch, S. (2018). Molecular mechanisms of long noncoding RNAs and their role in disease pathogenesis. *Oncotarget*, *9*(26), 18648–18663. https://doi.org/10.18632/oncotarget.24307

Khoo, S. K., Petillo, D., Kang, U. J., Resau, J. H., Berryhill, B., Linder, J., Forsgren, L., Neuman, L. A., & Tan, A. C. (2012). Plasma-based circulating MicroRNA biomarkers for Parkinson's disease. *Journal of Parkinson's disease*, *2*(4), 321–331. https://doi.org/10.3233/JPD-012144

Liu, W., Zhang, Q., Zhang, J., Pan, W., Zhao, J., & Xu, Y. (2017). Long non-coding RNA MALAT1 contributes to cell apoptosis by sponging miR-124 in Parkinson disease. *Cell & bioscience*, *7*, 19. https://doi.org/10.1186/s13578-017-0147-5

Sakai, A., & Suzuki, H. (2014). Emerging roles of microRNAs in chronic pain. *Neurochemistry international*, *77*, 58–67. https://doi.org/10.1016/j.neuint.2014.05.010

Vallelunga, A., Ragusa, M., Di Mauro, S., Iannitti, T., Pilleri, M., Biundo, R., Weis, L., Di Pietro, C., De Iuliis, A., Nicoletti, A., Zappia, M., Purrello, M., & Antonini, A. (2014). Identification of circulating microRNAs for the differential diagnosis of Parkinson's disease and Multiple System Atrophy. *Frontiers in cellular neuroscience*, *8*, 156. https://doi.org/10.3389/fncel.2014.00156

Xu, D., Ma, X., Sun, C., Han, J., Zhou, C., Chan, M. T. V., & Wu, W. K. K. (2021). Emerging roles of circular RNAs in neuropathic pain. *Cell proliferation*, *54*(12), e13139. https://doi.org/10.1111/cpr.13139

Zhang, F., Yao, Y., Miao, N., Wang, N., Xu, X., & Yang, C. (2022). Neuroprotective effects of microRNA 124 in Parkinson's disease mice. *Archives of gerontology and geriatrics*, *99*, 104588. https://doi.org/10.1016/j.archger.2021.104588

Zhang, M., & Bian, Z. (2021). Alzheimer's Disease and microRNA-132: A Widespread Pathological Factor and Potential Therapeutic Target. *Frontiers in neuroscience*, *15*, 687973. https://doi.org/10.3389/fnins.2021.687973