Original Article

Analysis of key lncRNA related to Parkinson's disease based on gene co-expression weight networks

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ABSTRACT

الأهداف: تحديد RNAs الرئيسية غير المشفرة (lncRNAs) ذات السلسلة الطويلة والمتعلقة بـ PD وتقديم منظور جديد حول دور lncRNAs في الفيزيولوجيا المرضية لمرض باركنسون (PD).

المنهجية: تضمنت دراستنا تحليل رقائق الجينات من المادة السوداء وخلايا الدم البيضاء، سواء الطبيعية أو الشاملة لـ PD، في قاعدة بيانات (GEO)، وذلك باستخدام تحليل شبكة التعبير الجيني المشترك الموزون (WGCNA). سهلت تقنية WGCNA فحص الجينات المعبر عنها تفاضليًا (DEGs) في المادة السوداء وخلايا الدم البيضاء للأفراد المصابين بـ PD. عند دمجها مع البيانات السريرية، تم اختيار وحدات الجينات التي تحتوي على تفاصيل سريرية مهمة لتكامل الشبكة في تحليل التخصيب GO وKEGG.

النتائج: وجدنا زوج من وحدات LncRNA. كان العنصر الحاسم في GSE7621 هو الوحدة الفيروزية. تم الحصول على DEGs باستخدام GSE133347. تركز وظائف GO على ربط فوسفاتيديلينوسيتول، والاستجابات الالتهابية، وتنظيم الأعصاب والمشابك العصبية. تم إثراء تحليلات KEGG إلى حد كبير ضمن مسارات إشارات P13K-Akt وFaxO وmTOR وOxytocin و cGMP-PKG. كشف مخطط Venn أن اثنين من LncRNA الرئيسيين هما CH17-189H20.1 وRP11-168O16.1.

الخلاصة: باستخدام طريقة WGCNA، حصلنا على وحدات مرتبطة بـ PD، وحددنا وحدات جينية ذات أهمية بيولوجية، وحصلنا على LncRNAs الأساسية، ووجدنا جينات مستهدفة محتملة لتحليل التخصيب. كان الهدف من بحثنا هو تطوير طرق علاج أكثر تفصيلاً وفعالية للـ LncRNAs المرتبطة بـ PD.

Objectives: To identify a key Long chain non-coding RNAs (lncRNAs) related to PD and provide a new perspective on the role of LncRNAs in Parkinson's disease (PD) pathophysiology.

Methods: Our study involved analyzing gene chips from the substantia nigra and white blood cells, both normal and PD-inclusive, in the Gene Expression Omnibus (GEO) database, utilizing a weighted gene co-expression network analysis (WGCNA). The technique of WGCNA facilitated the examination of differentially expressed genes (DEGs) in the substantia nigra and the white blood cells of individuals with PD. When merged with clinical data, gene modules containing crucial clinical details were chosen for network integration in GO and KEGG enrichment analysis.

Results: A pair of LncRNA modules were identified. The crucial component in GSE7621 was the turquoise module. The DEGs were acquired using GSE133347. GO functions focused on phosphatidylinositol phosphate binding, inflammatory responses, and the regulation of nerves and synapses. KEGG analyses were largely enriched within the P13K-Akt, FaxO, mTOR, Oxytocin, and cGMP-PKG signaling pathways. A Venn diagram revealed that the two key LncRNA were CH17-189H20.1 and RP11-168O16.1.

Conclusion: Using the WGCNA method, we obtained PD-related modules, identified biologically significant gene modules, obtained core LncRNAs, and found potential target genes for enrichment analysis. The objective of our research was to advance more detailed and efficient treatment methods for lncRNAs associated with PD.

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As the global population ages, there has been a rise in the occurrence of diseases associated with dementia. Parkinson disease (PD) holds the position as the second most prevalent neurodegenerative condition globally, following only Alzheimer's disease, and it's also a permanent, progressive neurodegenerative condition.[1,2] At present, the global prevalence rate for people over 60 years old is 1%, with a marginally higher occurrence in men compared to women.[3] The PD is defined by symptoms including resting tremors, bradykinesia, and stiffness, which reduce patients' quality of life and eventually result in profound disability related to the inability to control somatic movements.[4] Additionally, current treatment options can improve symptoms but cannot prevent disease progression. Consequently, discovering novel therapies is of paramount importance.[5] While the origins and development of PD are intricate, the deterioration of dopaminergic neurons stands out as a key pathological characteristic.[6] Delving deeply into the mechanisms of PD and identifying areas for intervention holds significant clinical value in managing PD's emergence and progression.

Long-chain non-coding RNAs (LncRNAs) represent a distinct category within RNA. Spanning 200-100,000 nucleotides, these entities lack the ability to encode proteins, possess distinct secondary structures, and exhibit both tissue-specific and spatio-temporal expression specificity.[7] Studies have shown that tens of thousands of human genome-encoded LncRNAs play a role in biological networks that regulate gene expression via transcription, post-transcription, and epigenetic mechanisms.[8] Within the central nervous system, a variety of tissue-specific lncRNA exhibit spatiotemporal expression patterns that are meticulously controlled, as well as cell type-specific and evolutionarily conserved features.[9] Irregular expression of lncRNA and/or genetic alterations may initiate multiple neurodegenerative disorders and conditions, PD included.[10,11] Briefly, identifying irregularly expressed circulating miRNAs and lncRNAs is crucial for the forcoming diagnosis and treatment of PD. A multitude of studies suggest that atypical lncrnas play a role in the pathological procession of PD. Kraus et al[12] found that 5 lncRNAs with significantly different expression were detected in the cingulate gyrus of midbrain tissues from PD patients, including significantly upregulated expression of H19 upstream conserved 1 and 2 and significantly downregulated expression of long intergenic noncoding RNA-p21 (lincRNA-p21), metastasis-associated lung adenocarcinoma transcript 1 (MALAT1), small nucleolar RNA host gene 1 (SNHG1), and trophoblast-derived noncoding RNA (TncRNA). Lv et al[13] reviewed that the role of lncRNAs in the pathophysiology of PD, the association with PD-linked genes, and the significance of lncRNAs as potential biomarkers and potential targets for PD treatment. Identifying the specific LncRNA involved in a given disease not only helps to clarify the pathology of the disease but also serves as a target for treatment.[14]

The emergence of high-throughput sequencing technologies like GeneChip RNA-Seq in recent years has led to the acquisition of extensive omics data. The exploration of relationships between gene expression, disease states, and functions has also been facilitated by data analysis and systematic research. Thus, gene microarray data may serve as a crucial tool in identifying the genes drive the genesis and development of PD.[15]

Our current research employed the Gene Expression Omnibus database (GEO database) along with weighted gene co-expression network analyses (WGCNA) for examining gene expression in PD. We screened hub genes closely related to PD using substantia nigra tissue samples[16,17] and blood cell samples. We then used GO enrichment analysis to functionally analyze our hub genes and examined KEGG signaling pathways to study the link among the central genes and the occurrence and development of PD. Our study helped reveal the regulatory mechanisms of certain signaling pathways. The results of our study could also contribute to creating a system for assessing and forecasting PD diagnoses, decreasing the disease's occurrence and severity, and pinpointing possible treatment targets.

Methods.

Ethical statement. Ethical approval for the study was obtained from the Medical Ethics Committee of Beijing Shijingshan Hospital

Data Sources. Data for the bioinformatics analysis of GSE7621 and GSE133347 were gathered from the National Center for Biotechnology Information (NCBI) public data platform GEO (Gene Expression Omnibus) database. The data was analyxed through arry-based expression profiling, focusing on homo sapiens as the speices. The GSE7621 dataset represented post-morbid substantia nigra tissue information from patients with PD. The platform was GPL19109 [HG-U133_Plus_2] Affymetrix Human Genome U133 Plus 2.0 Array, which included 16 PD patients and nine normal

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patients. GSE133347 was PD white blood cell data. The platform was GPL21047 Agilent-074348 Human LncRNA v6 4X180K [Probe Name Version], and included five PD patients and 5 normal patients.

Data processing and analysis of differentially expressed genes (DEGs). Utilizing the R software package, the initial data set underwent preccessing, with background correction standardizations and expression value calculations were performed on the original data using the RMA algorithm.[18] To distinguish between lncRNA and mRNA within the GSE7621 dataset, we re-annotated the chip probe. The BioMart package in R was used to annotate and distinguish LncRNA from the ensembl database.[19] Then DEGs between the 2 groups in the GSE7621 and GSE133347 datasets were analyzed, respectively, using the limma package in R (p-value<0.05, FC>1.5 or FC<0.667).[20]

WGCNA. The WGCNA is a widely used modular analysis technique that has been applied manytimes to recognize and screen biomarkers of or drug targets for complex diseases.[21] We first completed quality inspection and outlier analysis on the gene expression of the samples to ensure that they were all samples that could be used properly. Furthermore, a network for co-expressing genes was developed utilizing the WGCNA package in the R software.[22,23] Subsequently, we constructed a correlation matrix linking the 2 genes, utilizing the primary connection relationship and the Pearson correlation matrix, and analyzed the network topology to calculate the size of the soft threshold. The soft threshold is based on the criterion of approximating scale-free topology. The index curve of the scale-free topological fit flattens out after it reaches higher values, and the selected soft threshold must also needs to enhance its average connectivity. The adjacency network was further converted into a topological overlap matrix (TOM). The TOMs are capable of assessing a gene's network interconnectivity and are instrumental in creating networks (defined as the sum of its neighbors with all other genes).[24,25] We

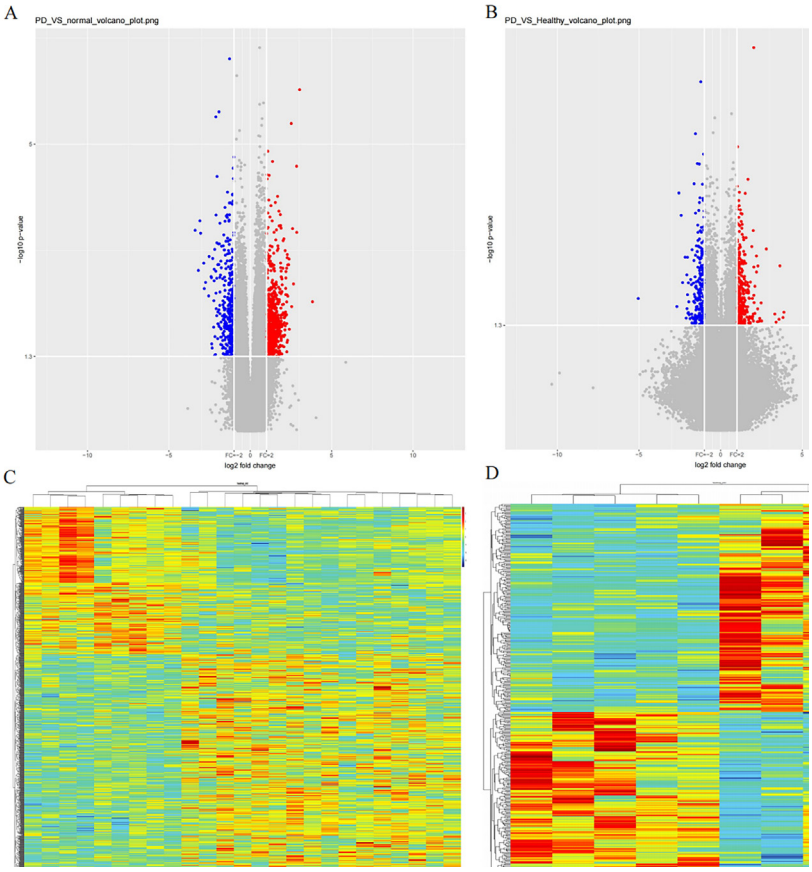

Figure 1 - Differentially expressed genes (DEGs) in PD tissues. **A, B**) Volcano plots showed the distribution of DEGs in GSE7621[a] and GSE133347 **B,C, D**) Heatmaps show the significantly up- and downregulated DEGs in **C**) GSE7621 and **D**) GSE133347.

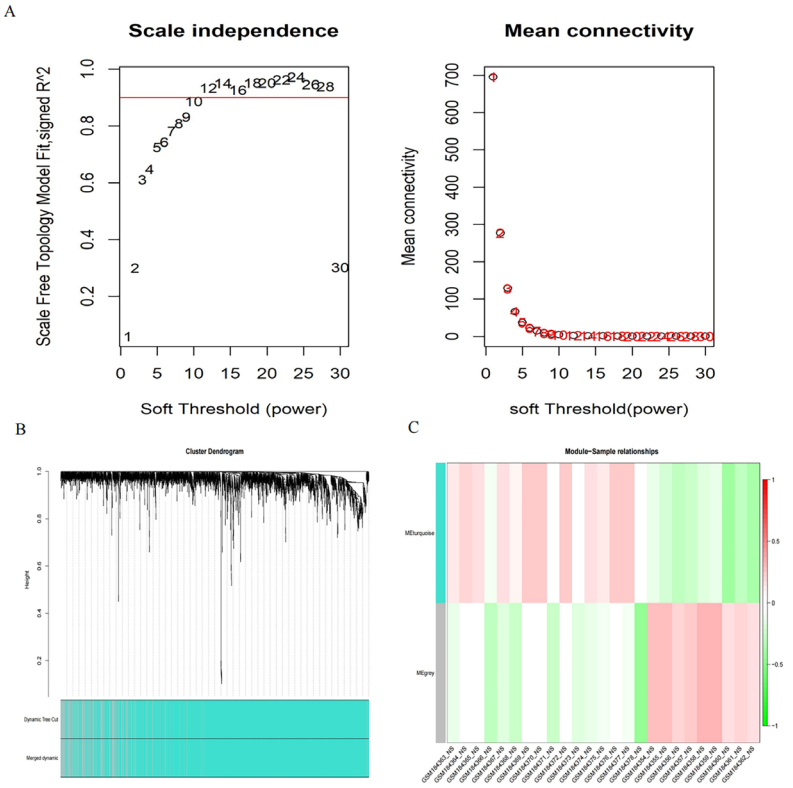

Figure 2 - Construction of weighted gene co-expression network. **A**) Analysis of network topology for soft thresholding parameters, **B**) Gene clustering tree obtained by hierarchies of adjacency-based dissimilarities; **C**) Adjacency identification of clinical features combined with modular genes.

performed average association stratification using the TOM-based difference metric, which classified genes exhibiting comparable expression patterns into their respective gene modules.[22,23] After module identification, according to the phenotypic data from each group, the t-test was employed to determine the *p*-value for each group's gene expression significance test. Each module's importance was determined as the average value of the gene significance within the module. The existence of specific diseases was related to further analysis of the modules. We calculated the significant differences in module eigengenes (MEs), selected a tangent line for the module tree diagram, and merged some of the modules.

Feature module and Hub gene screening. During each gene module's principal component analysis (PCA), gene expression patterns were consolidated into individual characteristic expression profiles within a specific module, with MEs serving as the primary components. Pearson correlation tests were also employed to assess the relationship between MEs and diseases, aiming to identify the pertinent modules, and to select modules that were highly correlated with PD for further analysis. Moreover, to locate the modules associated with the onset of PD, we conducted Pearson correlation analysis between the modules and PD to identify Hub genes. Our selection of the data set was based on its disease modle's highest correlation coefficient, a module that stood out as the largest across all the modules. The exact magnitude of Pearson's correlation was gauged within the module linkage established by the module and its related Hub genes. For pinpointing the primary target genes, differential gene analysis was conducted on the dataset, utilizing a VENN map to locate genes related to PD in the genes that showed varied expression in normal and PD tissue samples in GSE7621, as well as in normal and white blood cell samples in GSE133347. Two crucial LncRNAs, CH17-189H20.1 and RP11-168O16.1, were excluded from our analysis.

Gene set enrichment analysis. In the functional analysis of high-throughput gene data, the enhancement of the Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways is widely utilized. The DAVID database offers an extensive array of tools for functional annotation, enabling researchers to delve into the biology of a vast array of genes and comprehend their consequences.[26] This research utilized

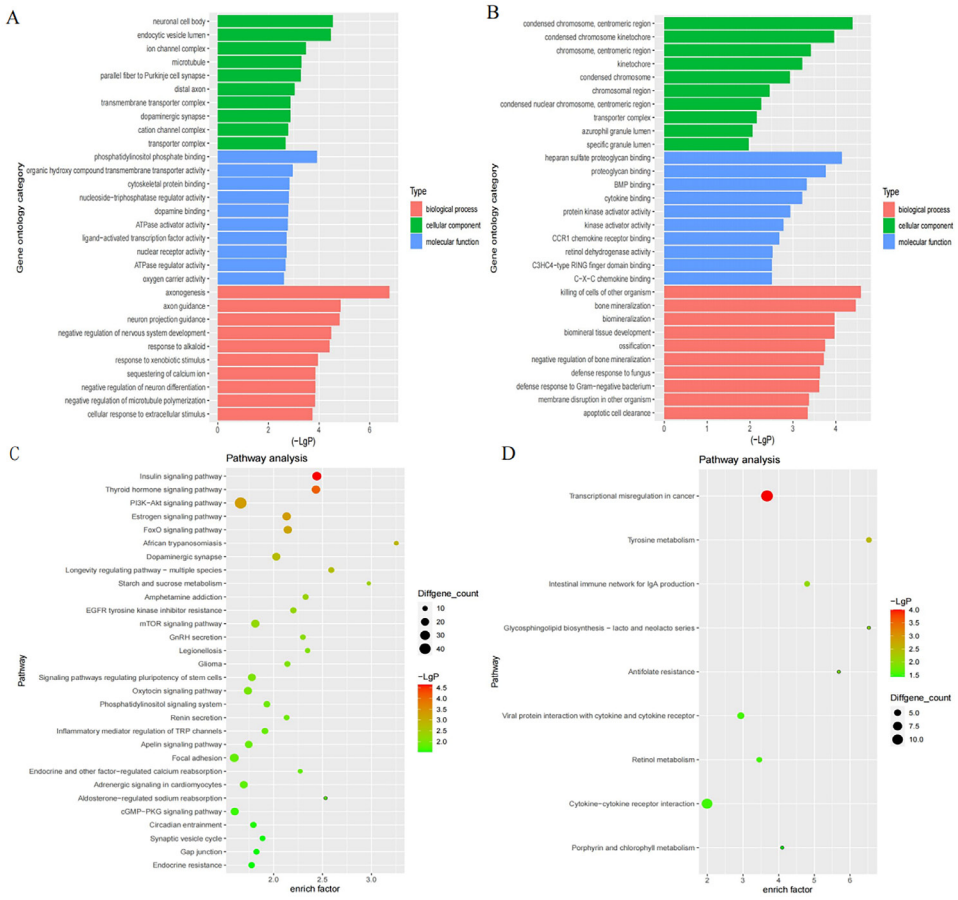

Figure 3 - GO enrichment and KEGG signaling pathway analyses. **A**) GO enrichment analysis of genes in the Turquoise module; **B**) GO enrichment analysis of DEGs between patients and normal samples in GSE133347; **C**) KEGG signaling pathway analysis of genes in the Turquoise module; **D**) KEGG signaling pathway analysis of DEGs between patients and normal samples in GSE133347.

the DAVID database to analyze GO enrichment annotations in crucial modules, encompassing biological process (BP), cellular component (CC), molecular function (MF), and KEGG pathway enrichment analysis.

Protein-protein interaction (PPI) analysis. The STRING 11.0 database (http://string-db.org/) for Retrieval of Interacting Genes/Proteins consists of a collection of established or forecasted protein interaction information. In the present study, we performed direct and indirect PPI network analysis of DEGs in PD using STRING 11. 0. The construction of PPI networks was carried out using Cytoscape software, adhering to these specific data conditions: a minimum necessary interaction score exceeding 0.4. Post-export of the analysis outcomes, the Degree values were arranged in a descending sequence using Microsoft Office Excel 2007, and the top 15 genes (Degree>5) were excluded as central genes.

Identification and validation of core genes. By identifying overlapping genes that were both key module genes in the GSE7621 dataset and DEGs in the GSE133347 dataset, we screened out two key lncRNAs CH17-189H20.1 and RP11-168O16.1 for further analysis. Key gene expressions in PD and normal tissues underwent revalidation through the ggpub and ggplot2 software tools. The pROC software package was employed to graph ROC curves, evaluating the diagnostic significance of crucial genes and forecasting the ideal threshold for PD.

Results. ***DEG analysis.*** Following the initial processing of the data, lncRNAs with varying expressions were excluded from the datasets GSE7621 and GSE133347. R software was used to draw volcano plots and heatmaps, and DEGs between the 16 PD patients and nine normal patients in the GSE7621 dataset and DEGs between the five PD patients and 5

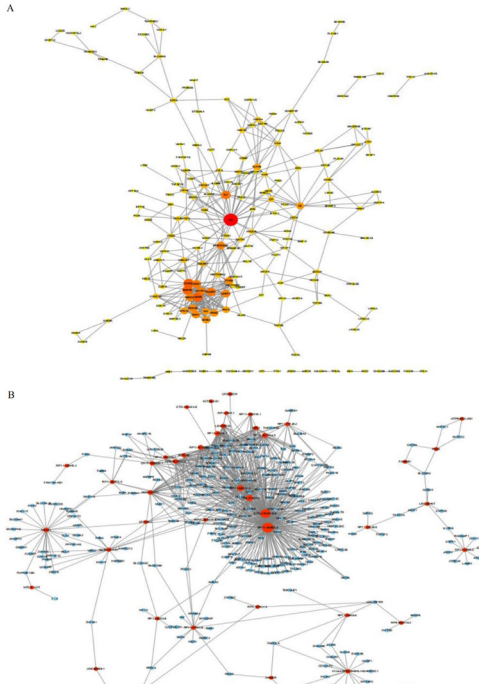

Figure 4 - Cytoscape-Generated PPI Network. **A**) PPT network of Turquoise module genes; **B**) PPI network of DEGs in GSE133347.

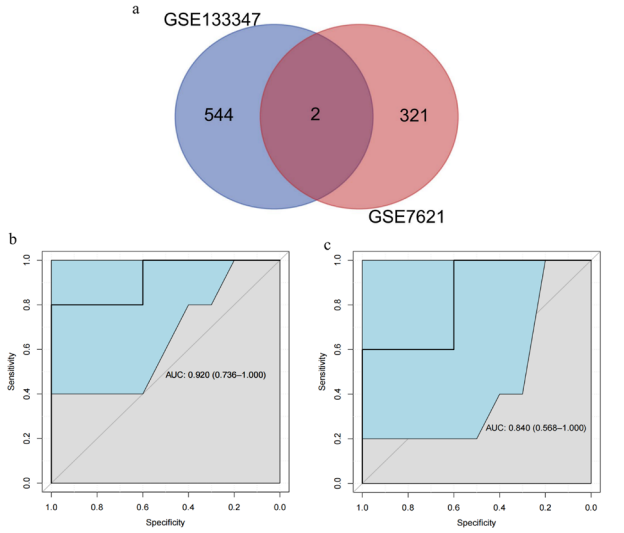

Figure 5 - Identification and validation of key genes. **A**) Venn diagram of common gene analysis between Turquoise module genes and DEGs in GSE133347. **B-C**) ROC curves of key genes. B) for CH17-189H20.1z and RP11-168O16.1

normal patients in the GSE133347 dataset are shown in **Figure 1**. The volcano plots illustrate the distribution of DEGs (**Figure 1a, b**), and the heatmaps show the results of bidirectional hierarchical clustering of DEGs and samples (**Figure 1c, d**).

Construction of weighted gene co-expression networks. The GSE7621 data set was analyzed using the WGCNA algorithm. Based on scale-free network distribution fitting, β=12 was selected as the soft threshold of this data-set (**Figure 2a**). We then calculated the adjacency matrix between genes and the topological overlap TOM and constructed a stratification between genes based on a TOM Clustering tree. The dynamic shearing tree method merged the modules with higher MEs similarity and eventually clustered genes into two modules, the Turquoise module and the Grey module (**Figure 2b**). Finally, correlations between further co-expression modules and clinical phenotype Sexual heat map analyses (**Figure 2c**) showed that the Turquoise module had the greatest correlation with PD (r=1, p=0.000).

The GO and KEGG Pathway enrichment analysis. After GO enrichment analysis, we obtained the detailed functions of the Turquoise module (**Figure 3a**), and found that the genes in this module were mainly present in neuronal cell bodies and endocytic vesicle lumens, and were involved in phosphatidylinositol phosphate binding, organic hydroxy compound transmembrane transporter activity, axonogenesis, neuron projection and guidance, and negative regulation of nervous system development. It's possible that these roles are linked to the emergence of PD. The DEGs in the GSE133347 dataset were mainly involved in molecular functions and biological processes, including killing foreign cells, biomineral tissue development, biomineralization, regulating mitotic nuclear division, cellular killing, and cellular responses to tumor necrosis factor (**Figure 3b**). Additionally, we conducted an analysis of KEGG pathway enrichment analysis on the DEGs within the Turquoise module and the GSE133347 dataset (**Figures 3c and 3d**), discovering an enrichment of genes in the Turquoise module across various signaling pathways including P13K-Akt, FaxO, Dopaminergic synapses, longevity regulation, resistance to EGFR tyrosine kinase inhibitors, mTOR, oxytocin, cGMP-PKG, and other KEGG signaling routes.

The PPI analysis. We performed PPI analysis on the genes in the Turquoise module and the DEGs in the GSE133347 dataset using STRING 11.0 and Cytoscape software. We analyzed and listed the central node proteins of the first 15 protein interaction networks. For the Turquoise module genes, the order was RP11-548B3.3, CTD-2292M16.8, LA16c-314G4.4, RP11-88H12.2, RP11-531A24.3, RP11-521D12.1, CTD-2527I21.4, RP11-433J8.1, MUC20-OT1, NEAT1, LINC00632,

NBR2, CH17-189H20.1, RFPL3S, NUTM2A-AS1 (**Figure 4a**). For the DEGs in the GSE133347 dataset, the order was IL6, AURKA, CDC20, BUB1B, IL4, HJURP, FOXM1, BIRC5, CENPU, HIST2H2BE, UHRF1, TYMS, CDCA5, SKA1, RRM2, GINS2, TK1, SPC25, CN, ELANE, ANL (**Figure 4b**).

Identification and validation of key genes. To further ensure that the genes in the Turquoise module were associated with the occurrence of PD, we further used VENN analysis to intersect the genes in the module and the DEGs screened in the GSE133347 dataset. In the end, we identified two genes, CH17-189H20.1 and RP11-168O16.1, as core target genes (**Figure 5a**). Following this, we conducted a ROC analysis to ascertain the diagnostic significance of the two principal genes and the best cut-off value for predicting PD at the gene expression level (**Figure 5b, c**). Findings indicate a potential inbolvement of these two crucial genes in the emergence of PD.

Discussion. At present, the development of PD is believed to be extremely complicated,[27] linked to a variety of causes including genetics, aging, environmental influences, oxidative stress, and mitochondrial malfunction,[28] as well as to excessive protein production and clustering, neural inflammation, and impaired Ca2+ homeostasis.[29,30] The pathogenesis of the disease is also believed to be complex and involves pathophysiological changes in multiple organ systems.[31] To discover more specific therapies for PD, a deeper comprehension of the fundamental biological processes that propel the disease's progression and the influence of genetic control is essential. Research indicates a high presence of LncRNAs in the brains of mammals, serving various roles such as creating synapses for the development and diversification of neurons, as well as sustaining learning, cognitive functions, and memory functions.[11] As an instance, Kraus TFJ et al[32] found a notable increase in Snhg1 expression among PD patients, suggesting Snhg1's crucial involvement in PD's emergence and progression. Research also indicates that LncRNA Snhg1, a type of ceRNA, controls the expression of associated genes after transcription. As an illustration, it has the ability to attach itself directly to miR-15b-5p, thereby reducing its expression. It has also been demonstrated to enhance the downstream target gene seven in absentia homolog 1 (SIAH1) of miR-15b-5p. The presence of this expression led to the clustering of α-syn, triggered the creation of Lewy bodies, and exacerbated pathological harm in PD.[33] It has been demonstrated that Snhg1 counteracts miR-15b-5p's impact on glycogen synthase kinase-3β(GSK-3β), thereby facilitating the formation of reactive oxygen species (ROS), obstructing autophagy, and hastening the emergence and progression of PD,[33] signifying its crucial involvement in PD's development. Li et al[34] claimed that upregulated NEAT1 promoted the PD modles' autophagy, apoptosis, inflammation, cytotoxicity, oxidative stress, and ferroptosis, while also reducing cell survival. Huang et al.[35] revealed a decrease in lncRNA MEG3 levels in PD, potentially influencing LRRK2 expression to control cell survival and apoptosis associated with PD. Previous studies[13] found that some lncRNA protection (like UCHL1, MAPT AS1 and Mirt2), while others, including HOTAIR, MALAT1, NEAT1, lincrna p21, and SNHG1, may worsen the condition of PD.

The majority of earlier research, on the other hand, concentrated solely on individual genes, thereby offering only limited insights into the biological mechanisms behind PD. The WGCNA, in contrast, treats genes with similar functions, or those that appear in the same biological pathway, as a module. This allows for the construction of adjacency TOM between genes, the identification of highly synergistically changing genetic modules, the combination of clinical information, the analysis of the correlation between modules and clinical phenotypes, and the complete use of large-scale genomic data information in order to study groups of genes as a whole.[21]

Our study used the WGCNA method to screen the LncRNA modules that were significantly related to PD and then used the application of GO and KEGG pathway enrichment analysis to the LncRNA within the modules to reveal genetic interactions and potential pathways and mechanisms in PD. We identified 2 valid modules and found that one of the modules, the turquoise module, was significantly correlated with PD. We extracted the relevant target gene information for the turquoise module LncRNA, and visualized the network and clarified hub genes. While LncRNA is incapable of being converted into protein within a living organism, it plays a role in numerous cellular functions. Because of its tissue specificity, LncRNA are widely applied to research on molecular targets and markers. Many LncRNAs are only located in the nucleus and regulate gene expression, however, they have the potential to disrupt genes via diverse methods.

In the turquoise module, the LncRNAs predominantly showed an increase in phosphatidylinositol phosphate binding, the creation of nerves and synapses, pathways for inflammatory response signaling, and various other functions associated with the nervous system's development and upkeep. Previous studies have shown

that traditional models of mammalian neurodegeneration were often limited by futile axonogenesis with minimal functional recovery of severed neurons.[36] Our research also revealed the involvement of our principal lncRNA in various signaling pathways, including P13K-Akt, FaxO, dopaminergic synapse formation, longevity control, resistance to EGFR tyrosine kinase inhibitors, mTOR, oxytocin, and cGMP-PKG signaling pathways.

Many of these pathways and functions could be tied to the development of PD. The PI3K/Akt/mTOR route significance influence myelination,[37] with Forkhead box O (FoxO) transcription factors being subsequent targets of the serine/threonine protein kinase B (PKB)/Akt.[38] Akt kinase plays a crucial role in controlling cell growth and survival. The Phosphorylation of FoxOs by Akt suppresses their transcriptional activities, thereby enhancing cell survival, growth, and proliferation. The depletion of dopaminergic neurons is a key factor in the pathogenesis of PD, leading to clinical manifestations in PD patients when over 80% of the dopaminergic neurons in the substantia nigra compact area (SNpc) are lost.[39] In the realm of neurodegenerative diseases PD, the mechanistic (protp-mammalian) target of rapamycin (mTOR) stands as a crucial pathway.[40] These pathways associated with longevity are linked to various processes, such as cognition, metabolism, brain plasticity, and stress responses. mTOR regulates autophagy, apoptosis, and mitochondrial energy metabolism, making it crucial in the processes of aging and neurodegenerative diseases. Numerous studies have found that the cGMP/PKG pathway helps prevent the activation of the pre-apoptotic pathway, and thus promotes neuronal cell survival.[41] Finally, the Oxytocin signaling pathway is one of the possible causes of PD disease.[28] These pathways explain the relationship between LncRNA target genes and PD and provide new directions for future PD research.

We also constructed a protein-protein interaction network for key modules. We then screened out PD-specific LncRNAs based on blood leukocyte samples from PD patients. The primary enrichment of these LncRNAs was in their molecular roles and biological activities related to immune system regulation and pathways signaling inflammatory responses. By intersecting the hub genes in the key module and the DEGs screened from the PD leukocyte samples, we evaluated 2 key hub lncRNAs: CH17-189H20.1 and RP11-168O16.1. The ROC analysis showed that these 2 genes had good diagnostic value in PD.

To our knowledge, this research is pioneering in integrating WGCNA with PD-associated lncRNA. Despite the identification of certain lncRNAs linked to PD through advanced sequencing techniques by scientists, additional confirmation of these lncRNAs' molecular processes is required. The cost of sequencing technology is high. Additionally, the existing databases fall short in accurately measuring the function of lncRNAs in PD. Verifying lncRNA's function in the diagnosis and treatment of PD necessitates further studies to comprehensively understand lncRNA's structure and functionality. Gene or cell therapies targeting lncRNAs may have unknown adverse effects, and clinical trial data on off-target effects are lacking. In summary, our study still has several limitations. Firstly, probe re-annotation helpd us obtain reliable LncRNA data from the previous GEO chips. However, due to different sequencing platforms within the chip and different update iterations, the probe re-annotation method did not cover all LncRNAs. Secondly, our conclusions still need to be verified with cellular and molecular experiments to understand whether the lncRNAs we detected are actually causally related to PD. Thirdly, our study's sample size was quite limited, necessitating more extensive samples for confirming our results. The data were externally verified and the relevant machine learning algorithm was used to find important target lncRNA. Fourthly, the clinical data related to our samples were incomplete, and our results would be more meaningful if we had more specific clinical parameters available for PD patients. To sum up, lncRNA expression is important for PD, which is expected to provide more individualized and precise diagnosis and treatment for PD patients.

Currently, identifying clinical PD cases largely hinges on symptomatology, with current treatment approaches proving effective only during the disease's initial phase. Although many therapeutic strategies for PD are being vigorously developed, there is no neuroprotective therapy to treat or prevent the progression of PD. A variety of small interfering Rnas and antisense oligonucleotides have received authorization for addressing conditions associated with the liver, muscles, and central nervous system.[42] However, due to the specificity, targeted delivery and low immune reactions such as obstacle, there is currently no treatment method based on lncRNA in clinical development. Previous work had identified several LncRNAs that may be closely related to the pathogenesis of PD but had not yet studied the core PD-related LncRNA that we identified in this study. Consequently, the possible LncRNA factors we pinpointed are crucial for comprehending PD's development and offer prospective focal points for upcoming PD studies. In summary, we combined weighted gene co-expression network analysis and PD tissue and blood samples to identify PD-related

LncRNA, obtained core LncRNA, and performed GO and KEGG Pathway enrichment analysis on these LncRNAs. The results of our study shed fresh light on lncRNA's function in PD's development, suggesting that the crucial lncRNAs CH17-189H20.1 and RP11-168O16.1 could play a pivotal role in these diseases' progression and hold significant promise as targets for treatment and diagnosis. Undoubtedly, the pathogenesis of PD remains comlpex, necessitating additional research to precisely elucidate the cellular and molecular processes of two crucial lncRNAs and other elements implicated in PD.

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