GENETIC BIOMARKERS IN PARKINSON'S DISEASE

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Summary

Parkinson's disease (PD) is a neurodegenerative condition that involves the gradual loss of dopaminergic neurons in the substantia nigra. The discovery of genetic biomarkers has greatly enhanced our comprehension of the etiology of Parkinson's disease (PD), providing valuable knowledge about the molecular pathways that drive the disease and creating opportunities for improved diagnosis, prognosis, and focused treatment. Genetic investigations have identified several crucial genes linked to Parkinson's disease (PD), such as LRRK2, SNCA, GBA, PARK2 (Parkin), PINK1, and PARK7 (DJ-1), among others. The presence of mutations in these genes emphasizes the significance of protein aggregation, mitochondrial dysfunction, lysosomal processing, and oxidative stress in the etiology of Parkinson's disease (PD). For example, mutations in the LRRK2 and SNCA genes are associated with both familial and sporadic cases of Parkinson's disease (PD), highlighting the importance of alpha-synuclein aggregation and kinase activity. GBA mutations, which are commonly linked to Gaucher's disease, have been found to be important risk factors for the development of PD. This highlights the role of lysosomal dysfunction in contributing to the disease.

Recent progress in the fields of genomics and bioinformatics has made it easier to identify more genetic variables and pathways that have a role in Parkinson's disease (PD). These genes encompass those associated with immunological response, cellular adhesion, dopamine production, and mitochondrial quality control. These findings not only improve our comprehension of the diverse genetic characteristics of PD but also emphasize the intricate interplay between genetic vulnerability and environmental factors in the progression of the disease.

Discovering genetic biomarkers for PD has potential for enhancing the therapeutic treatment of the disease. Genetic screening can assist in the early detection of diseases, enabling the implementation of neuroprotective treatments prior to the occurrence of substantial neurodegeneration. Moreover, comprehending the genetic foundation of PD facilitates the creation of individualized medical strategies that focus on certain pathways modified by genetic mutations in affected individuals.

Keywords:Parkinson's disease , biomarkes, genetic biomarkers, genes , mutations, genetic screening

Research on genetic indicators of PD is advancing quickly, with important implications for the diagnosis, prognosis, and therapy of the illness. Subsequent research should prioritize the examination of the functional nature The important step in understanding the complicated causes of Parkinson's disease (PD) and creating successful treatments is the thorough examination of discovered genetic variations and their interplay with environmental factors.

ΓΕΝΕΤΙΚΟΙ ΒΙΟΔΕΙΚΤΕΣ ΣΤΗ ΝΟΣΟ ΠΑΡΚΙΝΣΟΝ

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Περίληψη

Η νόσος του Πάρκινσον (PD είναι μια νευροεκφυλιστική διαταραχή που χαρακτηρίζεται από την προοδευτική απώλεια ντοπαμινεργικών νευρώνων στη μέλαινα ουσία. Ο εντοπισμός γενετικών βιοδεικτών έχει βελτιώσει σημαντικά την κατανόησή μας για την παθογένεια της PD, προσφέροντας γνώσεις για τους μοριακούς μηχανισμούς που βρίσκονται στη βάση της νόσου και ανοίγοντας νέους δρόμους για διάγνωση, πρόγνωση και στοχευμένη θεραπεία.

Γενετικές μελέτες έχουν αποκαλύψει πολλά βασικά γονίδια που σχετίζονται με την PD, συμπεριλαμβανομένων των LRRK2, SNCA, GBA, PARK2 (Parkin), PINK1 και PARK7 (DJ-1) μεταξύ άλλων. Οι μεταλλάξεις σε αυτά τα γονίδια υπογραμμίζουν τη σημασία της συσσώρευσης πρωτεϊνών, της μιτοχονδριακής δυσλειτουργίας, της λυσοσωμικής επεξεργασίας και του οξειδωτικού στρες στην παθοφυσιολογία της PD. Για παράδειγμα, οι μεταλλάξεις LRRK2 και SNCA εμπλέκονται σε οικογενείς και σποραδικές περιπτώσεις PD, δίνοντας έμφαση στο ρόλο της συσσωμάτωσης άλφα-συνουκλεΐνης και της δραστηριότητας κινάσης της LRRK2. Ομοίως, οι μεταλλάξεις GBA, γνωστές για τη συσχέτισή τους με τη νόσο του Gaucher, έχουν αναγνωριστεί ως σημαντικοί παράγοντες κινδύνου για την ανάπτυξη PD, υπογραμμίζοντας τη συμβολή της λυσοσωμικής δυσλειτουργίας στη νόσο.

Οι πρόσφατες εξελίξεις στη γονιδιωματική και τη βιοπληροφορική έχουν διευκολύνει την ανακάλυψη πρόσθετων γενετικών παραγόντων και οδών που εμπλέκονται στην PD. Αυτό περιλαμβάνει γονίδια που σχετίζονται με την ανοσολογική απόκριση, την κυτταρική προσκόλληση, τη βιοσύνθεση ντοπαμίνης και τον ποιοτικό έλεγχο των μιτοχονδρίων. Αυτές οι ανακαλύψεις όχι μόνο ενισχύουν την κατανόησή μας για τη γενετική ετερογένεια της PD αλλά τονίζουν επίσης την περίπλοκη αλληλεπίδραση μεταξύ της γενετικής ευαισθησίας και των περιβαλλοντικών παραγόντων στην ανάπτυξη της νόσου.
Ο εντοπισμός γενετικών βιοδεικτών για την PD υπόσχεται τη βελτίωση της κλινικής διαχείρισης της νόσου. Ο γενετικός έλεγχος μπορεί να βοηθήσει στην έγκαιρη διάγνωση, επιτρέποντας την έναρξη νευροπροστατευτικών θεραπειών πριν εμφανιστεί σημαντική νευροεκφύλιση. Επιπλέον, η κατανόηση της γενετικής βάσης της PD επιτρέπει την ανάπτυξη εξατομικευμένων ιατρικών προσεγγίσεων, στοχεύοντας συγκεκριμένα μονοπάτια που μεταβάλλονται από γενετικές μεταλλάξεις σε προσβεβλημένα άτομα.
Συμπερασματικά, η έρευνα για τους γενετικούς βιοδείκτες της PD εξελίσσεται ταχέως, με σημαντικές επιπτώσεις στη διάγνωση, την πρόγνωση και τη θεραπεία της νόσου. Μελλοντικές μελέτες που επικεντρώνονται στον λειτουργικό χαρακτηρισμό των αναγνωρισμένων γενετικών παραλλαγών και την αλληλεπίδρασή τους με περιβαλλοντικούς παράγοντες θα είναι κρίσιμες για την αποκάλυψη της πολύπλοκης αιτιολογίας της PD και την ανάπτυξη αποτελεσματικών θεραπευτικών στρατηγικών.

Λέξεις κλειδιά: Νόσος Parkinson, βιοδείκτες, γενετικοί βιοδείκτες, γονίδια, μεταλλάξεις, γενετικός έλεγχος

1.Introduction

Parkinson's disease is a neurodegenerative condition that gradually worsens over time. It is characterized by the gradual death of specific brain cells called dopaminergic neurons in a region of the brain called the substantia nigra. This cell death leads to the development of symptoms such as tremors, stiffness, and slowness of movement. Although the precise etiology of PD is still uncertain, it is widely accepted that a mix of genetic, environmental, and lifestyle variables play a role in its pathogenesis. Recent advancements in genetic research have provided valuable information on certain genetic markers that heighten the vulnerability to PD, providing fresh understanding of its development and prospective targets for treatment. Genetic factors contribute to over 25% of the risk linked to Parkinson's disease, and the genetic variations related with it differ in terms of both occurrence and risk level. Although uncommon, mutations occurring within specific genes (referred to as monogenic causes) can potentially contribute to the development of the condition. However, these mutations are typically identified through linkage analysis in families affected by the condition. Genome-wide association studies (GWASs) have identified several common genetic variations that have a minor impact on risk. These variants, such as GBA or LRRK2 variants, contribute to intermediate risk.

Familial Parkinson's disease, also known as monogenic PD, is distinguished by infrequent yet very influential genetic variations that elevate the likelihood of developing the condition. Autosomal dominant (for example, SNCAA53T and VPS35D620N) and recessive types of familial Parkinson's disease have been detected using linkage analysis in families, with the use of next-generation sequencing technology. However, it is important to note that only a small percentage, specifically 5-10%, of cases can be classified under this disease group. Genome-wide association studies (GWASs) have discovered low-penetrance genetic variants that are more commonly associated with sporadic Parkinson's disease, as opposed to high-penetrance variants. Initially, differentiating between familial and sporadic disease can assist in the identification of the disease, prediction of its course, and providing genetic guidance for family members who are at risk. Nevertheless, this categorization may mask the shared genetic or biological pathways that underlie both conditions.

2. Genetic basis of Parkinson's disease

2.1 The PARK genes and their influence

The identification of mutations in certain PARK genes has played a crucial role in comprehending the genetic foundation of Parkinson's disease (PD). The designation "PARK" for genes linked to Parkinson's disease (PD) is derived from a systematic nomenclature employed to discover and classify genes that, when altered, result in the onset of PD. The purpose of this naming approach is to systematically categorize the expanding roster of genetic variables that have been identified as contributors to the disease. Every gene associated with Parkinson's disease is given a distinct numerical identifier with the prefix "PARK", for example PARK1, PARK2, and so forth. This measurement aids in differentiating between several genes and mutations that contribute to the development of Parkinson's disease. The numerical sequence frequently corresponds to the chronological order in which these genes were identified or persistently linked to Parkinson's disease, regardless of their significance or role in the disease mechanism.

The PARK genes encompass a diverse array of functions and pathways, which include, but are not limited to, alpha-synuclein aggregation (e.g., SNCA/PARK1), mitochondrial function (e.g., PINK1/PARK6, PARK2/parkin), lysosomal function (e.g., GBA), and protein degradation (e.g., LRRK2/PARK8). The discovery and classification of these genes using the PARK nomenclature has played a crucial role in enhancing our comprehension of Parkinson's disease. This has provided valuable information about its molecular foundation and identified prospective targets for therapeutic treatment. PARK8, or the LRRK2 gene, is responsible for a significant number of cases of Parkinson's disease due to autosomal dominant mutations. LRRK2 mutations play a role in both familial and sporadic types of the disease, underscoring its significance in the pathogenesis of Parkinson's disease. Mutations in PARK1/4 have a significant impact on the protein alpha-synuclein, leading to the buildup of alpha-synuclein, which is a crucial characteristic of Parkinson's disease.

Autosomal recessive variants of Parkinson's disease (PD) are mostly linked to mutations in the PARK2/parkin gene, which are connected to mitochondrial malfunction and oxidative stress. Additional recessive mutations, such as those found in PARK6, PARK7 and additional PARK genes, further highlight the genetic diversity and complexity of PD.

We will provide a more comprehensive analysis of each gene and its specific contribution to the development of the disease.

The SNCA gene, which codes for the alpha-synuclein protein, has a key function in the development of Parkinson's disease (PD), a neurodegenerative condition marked by the gradual decline of dopaminergic neurons in the substantia nigra. This paper examines the intricate correlation between SNCA and PD, emphasizing the gene's structure, function, and the molecular mechanisms that explain its involvement in the disease.

2.2 Genetic variations and the risk of Parkinson's disease

2.2.1. SNCA

Alpha-synuclein, a protein produced by the SNCA gene, plays a crucial role in Parkinson's disease (PD) through both uncommon and frequent genetic variations. Autosomal dominant types of familial Parkinson's disease are linked to infrequent mutations, including p.A53T, p.A30P, and p.E46K. On the other hand, the SNCA rs356168 mutation, which is present in around 40% of people with European ancestry, has a less significant impact on the likelihood of developing the condition. These findings emphasize the significance of alpha-synuclein in the development of PD, namely its involvement in disease processes caused by the buildup of alpha-synuclein. The SNCA gene codes for a protein that weighs 14.5 kilodaltons and consists of 140 amino acids. This protein is produced from five exons and has a transcript length of 3,041 base pairs. SNCA is situated on chromosome 4q21.3-q22 and is a member of the synuclein protein family, which also contains beta-synuclein (SNCB) and gamma-synuclein (SNCG). The alpha-synuclein protein contains an area at the beginning called the N-terminal region, which has repetitive motifs known as KXKEGV. It also has a region called the non-Aβ component (NAC) region, which is very hydrophobic. Lastly, there is a portion at the end called the C-terminal region, which is acidic. The structural flexibility of this entity enables it to exist in two different forms: either as a disordered single unit or as a folded arrangement of four helices. This challenges the previously accepted notion that its single unit form is inherently hazardous. Alpha-synuclein is predominantly located in the brain, although it can also be detected in the heart, skeletal muscle, and pancreas. The precise biological role of it is not well understood, however various possibilities have been suggested. These functions encompass the regulation of dopamine, the promotion of tau protein fibrillation, and the protection of non-dopaminergic neurons through the modulation of p53 expression and apoptosis-related genes. The characteristic of Parkinson's disease is the abnormal buildup of alpha-synuclein within neurons, which then spreads to other regions of the brain. This process encompasses multiple methods of intraneuronal transmission, resulting in extensive neurotoxicity. SNCA plays a vital role in the development of PD, making it a key focus for therapeutic intervention and research. Gaining a clear understanding of the specific pathways via which SNCA mutations cause PD can help in the development of focused treatments that attempt to reduce the harmful consequences of alpha-synuclein buildup. Moreover, a deeper understanding of the evolutionary adaptations of SNCA could provide valuable knowledge for manipulating its function in a therapeutic setting, perhaps presenting novel approaches for the treatment or prevention of Parkinson's disease.

Ultimately, the SNCA gene and its corresponding protein, alpha-synuclein, are crucial to the investigation of Parkinson's disease. The presence of genetic variations in the SNCA gene has a considerable impact on the chance of developing Parkinson's disease, indicating the important role of the protein in the processes of the disease. Ongoing study into the genetic, structural, and functional features of alpha-synuclein holds the potential to reveal new

therapeutic solutions, despite the obstacles in completely understanding its roles and hazardous forms.

LRRK2

The presence of LRRK2 gene mutations has a significant role in both familial and sporadic cases of Parkinson's disease (PD), making it a crucial field of study for understanding the genetic variables that contribute to this neurodegenerative disorder. LRRK2 mutations are linked to around 5-12% of familial PD cases and 1-5% of sporadic PD cases, underscoring their significance in the genetic makeup of the disease. So far, scientists have discovered seven missense variants in LRRK2 that are known to cause disease. These mutations are R1441G, R1441C, R1441H, Y1699C, G2019S, R1628P, G2385R, and I2020T. These mutations occur in different functional regions of the protein, and some, like the G2019S mutation, cause the kinase activity of LRRK2 to become activated.

The G2019S mutation, in particular, stands out due to the high prevalence in certain populations, accounting for 36% of familial and sporadic PD cases among North African Arabs and about 30% in Ashkenazi Jewish communities. Conversely, it is significantly less common in European and North American populations and nearly non-existent in Asian ethnicities. Additional variants, such as G2385R and R1628P, demonstrate a strong correlation with the risk of Parkinson's disease (PD) in Asian populations. This emphasizes the influence of ethnicity and geographic location on the likelihood of developing LRRK2-related PD. Although there are genetic variations, the clinical and neurochemical characteristics of Parkinson's disease (PD) linked to LRRK2 mutations are remarkably comparable to those observed in idiopathic PD. Patients exhibit degeneration of dopaminergic neurons and inflammation in the substantia nigra compacta (SNpc), decreased levels of dopamine in the caudate pole, and the distinctive presence of Lewy bodies in the brainstem. Pathogenic mutations in LRRK2 impact many functional domains of the protein, causing changes in its normal enzymatic activity, specifically its kinase function. The G2019S mutation results in excessive stimulation of the kinase activity of LRRK2, indicating that the heightened activity of this enzyme may have a key function in the progression of PD. The specific molecular processes by which these mutations lead to neurodegeneration are currently being actively researched. Current ideas propose that these mutations affect neuronal autophagy, mitochondrial function, and cytoskeletal dynamics.

Gaining insight into the function of LRRK2 in Parkinson's disease (PD) provides new opportunities for therapeutic intervention. Targeting the kinase activity of LRRK2 offers a hopeful strategy for controlling the advancement of the disease. Multiple compounds that limit the kinase activity of LRRK2 are now being studied, providing potential for therapeutic interventions that may decelerate or halt the advancement of Parkinson's disease in individuals with these genetic abnormalities.

2.3 Genes that are inherited in an autosomal recessive manner

PINK1

The PINK1 gene, originally discovered by Unoki and Nakamura in 2001, consists of eight exonic regions that encode a serine/threonine protein kinase. This enzyme plays a vital part in the functioning of mitochondria and the metabolism of cellular energy, emphasizing the important role of mitochondria in maintaining the health of neuronal cells. According to the MDSGene database, there are 151 individuals worldwide who have been found to have PINK1 mutations. These mutations consist of 62 distinct variations. The PINK1 protein is mostly found in mitochondria, where it has a crucial function in maintaining mitochondrial quality control (mitoQC). This process entails the maintenance of robust mitochondrial networks and the removal of impaired mitochondria through mitophagy, an essential autophagic mechanism for maintaining cellular balance. The presence of mitochondrial malfunction is a defining characteristic of Parkinson's disease (PD), and the involvement of PINK1 in alleviating this dysfunction is crucial to its connection with the disease. In addition to its role in mitoQC, PINK1 demonstrates neuroprotective characteristics in response to different stressors, promoting cell survival and reducing neuronal demise. The dual role of PINK1 emphasizes the significance of this protein in preserving the overall well-being and ability to recover of cells, especially in the nervous system. The PINK1 protein possesses several key structural elements that play a crucial role in its localization and activity within mitochondria. These include an N-terminal mitochondrial targeting region, a transmembrane sequence, and a C-terminal domain.

Discovering PINK1 mutations in people with early-onset disease offers important understanding of how the disease develops and possible ways to intervene. Due to the enzyme's involvement in maintaining and protecting mitochondria from cell death, medications that try to improve PINK1 function or imitate its activity show potential as effective ways for slowing

down or stopping the progression of diseases.

Gaining a comprehensive understanding of the precise processes via which PINK1 mutations contribute to the onset of Parkinson's disease is of utmost importance in order to facilitate the development of medicines that specifically target these mechanisms. Contemporary studies concentrate on the restoration of mitochondrial function, the enhancement of mitophagy, and the protection of neuronal cells from damage caused by stress. Although there have been notable breakthroughs in comprehending the function of PINK1 in Parkinson's disease (PD), there are still various obstacles that need to be addressed. These include elucidating the full range of PINK1 mutations and their specific effects on mitochondrial function, developing effective therapies that targeting these molecular pathways and understanding the interaction between PINK1 and other genes involved in PD.

Parkin

Parkin is an E3 ubiquitin protein ligase that has a crucial function in directing proteins for destruction through the ubiquitin-proteasome system (UPS). The primary role of this function is crucial in preserving cellular homeostasis by the elimination of impaired or incorrectly folded proteins. The accumulation of such proteins might result in cellular malfunction and demise.

PRKN gene mutations are a prevalent hereditary cause of early-onset Parkinson's disease. Frequently, these genetic alterations cause a decrease in the functional ability of parkin enzymes, leading to the buildup of the substances that parkin normally acts upon and the specific demise of dopaminergic neurons in the substantia nigra, a characteristic feature of Parkinson's disease.

Parkin plays a crucial function not only in breaking down proteins but also in maintaining the quality of mitochondria through a process called mitophagy. Mitophagy is the process by which damaged or defective mitochondria are selectively broken down through autophagy, in order to effectively eliminate them and preserve the overall health of the cell. Parkin dysfunction, caused by genetic abnormalities, hinders the cell's capacity to eliminate dysfunctional mitochondria. The interruption can result in mitochondrial impairment, marked by decreased ATP synthesis, heightened oxidative stress, and the release of pro-apoptotic substances. These variables collectively contribute to the development of Parkinson's disease. Furthermore, parkin's function goes beyond mitochondria to encompass the control of other cellular mechanisms, such as inflammation, apoptosis, and certain components of the immunological response. Parkin's various functions emphasize its significance in maintaining cellular balance.

Gaining knowledge about the roles of parkin and the underlying mechanisms that cause its malfunction in Parkinson's disease (PD) provides opportunities for future therapeutic approaches. Potential treatment options could be explored through approaches that try to enhance parkin function, facilitate the clearance of damaged mitochondria, or duplicate its activities using pharmaceutical techniques. Furthermore, the field of research also includes gene therapy that focuses on rectifying PRKN mutations or enhancing its expression, which has great potential.

2.4 GBA

Glucocerebrosidase is an essential lysosomal enzyme responsible for the degradation and reutilization of glucocerebrosides, which are a specific form of glycolipid. GBA is essential for regulating cellular homeostasis and lipid metabolism by converting glycocerebrosides into ceramide and glucose. The presence of genetic abnormalities in the GBA gene leads to a dysfunctional GBA enzyme. This dysfunction causes glycocerebrosides to build up in lysosomes, which in turn impairs cellular function and contributes to the development of neurodegenerative diseases.

GBA gene mutations are connected to Gaucher disease, a type of lysosomal storage disorder, and have also been related with a higher likelihood of developing PD. The precise pathways via which GBA mutations contribute to Parkinson's disease (PD) are not well comprehended, but various possibilities have been put forward. These factors consist of altered autophagy-lysosomal pathways, heightened alpha-synuclein buildup caused by decreased lysosomal degradative ability, and intensified neuroinflammation and oxidative stress. The connection between GBA mutations and Parkinson's disease was discovered through studies made in families affected by Gaucher disease, which is a genetic illness that affects the lysosomes and is caused by mutations in the GBA gene. Researchers noted a higher occurrence of Parkinson's disease (PD) among individuals with Gaucher disease mutations, which prompted further investigations that confirmed GBA as a significant risk factor for developing PD. The discovery, occurring during the late 1990s and early 2000s, marked a significant change in scientists' understanding of the genetic makeup of Parkinson's disease.

GBA mutations are prevalent genetic risk factors for Parkinson's disease. Studies indicate that the prevalence of GBA gene mutations among individuals with Parkinson's disease in Western nations ranges from roughly 5% to 10%. The in-

cidence of this occurrence may be elevated in specific populations, particularly among Ashkenazi Jews, where the prevalence of GBA mutations among the general population is much higher. The discovery of GBA mutations as a risk factor for Parkinson's disease has had significant consequences for both research and clinical practice. The importance of lysosomal dysfunction and autophagy in the development of Parkinson's disease (PD) has been emphasized, broadening the scope of research in this area of PD beyond the dopaminergic system and alpha-synuclein pathology. This recognition has prompted the development of new therapeutic strategies aimed at enhancing lysosomal function, reducing alpha-synuclein accumulation, and improving mitochondrial health.

Clinically, the discovery of the GBA-PD link has led to increased interest in genetic testing and counseling services for people with PD and their families. It has also prompted research into the natural history and phenotype of GBA-associated PD, which is often characterized by earlier onset, faster progression, and greater likelihood of cognitive decline compared with PD without GBA mutations.

Conclusions

Studying monogenic types of PD is driven by the desire to apply molecular knowledge to understand the development of idiopathic PD. According to our current knowledge of the pathophysiology of PD, the main illness mechanism in both the idiopathic and hereditary types is the buildup of α-synuclein. The histopathological results in genetic forms exhibit greater variability and consist of tau pathology in LRRK2 cases, while most autopsied PRKN mutation carriers do not show α-synuclein accumulation. Further exploration of disease pathways is expected to result in a fusion of customized disease-altering treatments for each individual with Parkinson's disease. This can be likened to the symptomatic treatment of people with Parkinson's disease, where a tailored combination of antiparkinsonian medications is utilized to effectively manage the specific illness symptoms experienced by each patient.

There are several plausible causes for the absence of disease modification in Parkinson's disease (PD), including extensive degeneration at the time of diagnosis, varying involvement of individual disease mechanisms in PD patients, and a very brief observation period. The inclusion of study cohorts consisting of individuals with well-defined genetic characteristics is essential for the advancement of targeted medicines. Currently, there is ongoing research on medications that are based on genotype.

Nevertheless, genetic testing is not yet commonly incorporated into the process of diagnosing patients or selecting participants for clinical trials. Early consideration of genetic testing is crucial in the diagnostic care of patients with Parkinson's disease in order to address the limited timeframe available for implementing disease-modifying treatments. In certain fields, such as cancer treatment, the analysis of genetic variations has already become an integral part of clinical practice and has resulted in the creation of more effective clinical trials. The utilization of genetic testing will grow in significance for the therapeutic management of individuals with neurological conditions. For instance, the oligonucleotide medication that has recently been approved by the FDA Genetic testing of patients with spinal muscular atrophy is necessary for Nusinersen in order to determine the genetic diagnosis and evaluate patients' eligibility for clinical trials.

In order to further develop the effective strategy of targeted therapeutics in Parkinson's disease, it is necessary to have biomarkers that can categorize patients according to the cause of the underlying disease (such as identifying those with significant mitochondrial damage). Managing Parkinson's disease with medications that change its progression is challenging because there are no proven and dynamic biomarkers based on the underlying mechanisms. Genetic findings in Parkinson's disease (PD) have enhanced our comprehension of the clinical symptoms, the fundamental causes, and the possibility of specific treatments. While our current comprehension of disease biology is continuously growing, it is imperative that we promptly tackle the existing gaps in knowledge in the future. Performing genetic testing on individuals with "idiopathic" or "sporadic" Parkinson's disease is necessary to identify those who are eligible for genotype-based treatments. Stratifying research participants based on their genotype will increase the potential use of targeted medications.

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