

# Discovery of Highly Selective Kinase Inhibitors for the Treatment of Neurodegenerative Diseases

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## Abstract

Neurodegenerative diseases, such as Alzheimer's, Parkinson's and Huntington's disease, represent a significant and growing global health challenge. These disorders, characterized by the progressive degeneration of nerve cells, lead to debilitating cognitive and motor impairments. As the global population ages, the prevalence of neurodegenerative diseases is on the rise, making it imperative to develop effective therapeutic strategies. Recent advances in the field of drug discovery have paved the way for the development of highly selective kinase inhibitors, offering new hope for the treatment of neurodegenerative diseases. Kinases are a class of enzymes that play a crucial role in cell signaling and regulation. They are responsible for phosphorylating proteins, thereby activating or deactivating various cellular processes. Aberrant kinase activity has been implicated in several neurodegenerative diseases. Dysregulated kinases can lead to the accumulation of toxic protein aggregates, neuroinflammation and oxidative stress, all of which contribute to the progression of these diseases.

**Keywords:** Kinase inhibitors • Neurodegenerative diseases • Neuroinflammation

## Introduction

Targeting specific kinases involved in neurodegeneration offers a promising therapeutic approach. However, the challenge lies in developing highly selective kinase inhibitors that can modulate kinase activity without affecting essential cellular functions. Recent breakthroughs in drug discovery and molecular biology have enabled the design and development of such selective inhibitors. Selective inhibitors target specific kinases implicated in neurodegeneration while sparing other kinases necessary for normal cellular function. This selectivity minimizes off-target effects and reduces the risk of adverse reactions. Targeting specific kinases involved in disease pathways allows for precise modulation of the disease process, potentially leading to greater therapeutic efficacy. Selective kinase inhibitors can be tailored to target the specific kinase profiles of individual patients, enabling a personalized approach to treatment.

Mutations in the leucine-rich repeat kinase 2 (LRRK2) genes are associated with Parkinson's disease. Researchers have developed highly selective LRRK2 inhibitors that can potentially slow down disease progression. Cyclin-Dependent Kinase 5 (CDK5) is involved in the hyper phosphorylation of tau protein, a hallmark of Alzheimer's disease. Selective CDK5 inhibitors have shown promise in preclinical studies. Glycogen Synthase Kinase 3 $\beta$  (GSK3 $\beta$ ) is implicated in multiple neurodegenerative diseases, including Alzheimer's. Highly selective GSK3 $\beta$  inhibitors have been developed to target this kinase specifically. Mitogen-Activated Protein Kinases (MAPKs) play a role in neuroinflammation and cell death. Selective MAPK inhibitors are being investigated for their potential in mitigating neurodegenerative processes.

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Many neurodegenerative diseases have no cure and treatment primarily focuses on managing symptoms.

## Description

Medications, such as cholinesterase inhibitors for Alzheimer's disease or levodopa for Parkinson's disease, can temporarily alleviate cognitive or motor symptoms, respectively. Physical and occupational therapy play a crucial role in maintaining or improving the quality of life for individuals with neurodegenerative diseases. These therapies can help manage mobility issues, improve muscle strength and enhance daily functioning. Comprehensive care teams, including neurologists, nurses, social workers and psychologists, provide emotional and psychological support to patients and their families. Supportive care can improve coping strategies and enhance the overall well-being of individuals with neurodegenerative diseases. A healthy lifestyle, including a balanced diet, regular exercise and cognitive stimulation, may slow the progression of some neurodegenerative diseases and improve overall brain health. Researchers are continually investigating new drugs and therapies in clinical trials. Some experimental treatments aim to target specific disease mechanisms, such as beta-amyloid plaques in Alzheimer's disease or alpha-synuclein aggregates in Parkinson's disease.

Blood-Brain Barrier (BBB) Penetration is ensuring that these inhibitors can cross the BBB and reach their target in the brain is a crucial challenge. Safety Profiles involves rigorous safety testing is necessary to minimize the risk of unforeseen side effects and ensure the long-term safety of these inhibitors. Patient Stratification is identifying patients who would benefit most from selective kinase inhibitors based on their kinase profiles is a complex task that requires further research. Combination Therapies are combining selective kinase inhibitors with other therapeutic approaches, such as gene therapy or immunomodulation, may offer synergistic benefits. Disease-Modifying Therapies are one of the most significant challenges in neurodegenerative disease treatment is the development of disease-modifying therapies. These treatments aim to slow down or halt the underlying disease process rather than merely addressing symptoms. Immunotherapies are that antibodies and vaccines that target abnormal protein aggregates (e.g., beta-amyloid or tau in Alzheimer's) are being developed to clear toxic proteins from the brain. Gene Therapies are gene editing techniques, such as CRISPR-Cas9, are explored to correct genetic mutations responsible for diseases like Huntington's disease.

Stem Cell Therapies are stem cell-based approaches hold potential for replacing damaged or degenerating neurons. Induced Pluripotent Stem Cells

(iPSCs) can be generated from a patient's own cells and differentiated into neurons for transplantation. Neuroinflammation Modulation is the chronic inflammation in the brain is a common feature of neurodegenerative diseases. Researchers are investigating drugs that can modulate the immune response and reduce neuroinflammation as a potential treatment strategy. Precision Medicine is tailoring treatments to an individual's genetic and molecular profile is an emerging concept in neurodegenerative disease treatment. This approach can optimize treatment responses and minimize side effects. Lifestyle interventions, including dietary changes, exercise regimens and cognitive training, are being studied for their potential to slow disease progression and improve cognitive function [1-5].

## Conclusion

The discovery of highly selective kinase inhibitors represents a promising avenue for the treatment of neurodegenerative diseases. These inhibitors offer the potential for targeted and personalized therapies that could slow disease progression and improve the quality of life for affected individuals. While there are still challenges to overcome, the progress made in developing these inhibitors gives hope for a future where neurodegenerative diseases are more effectively managed or even cured. Continued research and collaboration between scientists, clinicians and pharmaceutical companies are essential to realize the full potential of selective kinase inhibitors in the fight against neurodegeneration. The treatment of neurodegenerative diseases remains a formidable challenge, but ongoing research offers hope for the development of more effective therapies. While current treatments primarily focus on managing symptoms, emerging approaches aim to modify the course of these devastating diseases. Disease-modifying therapies, stem cell-based treatments and precision medicine are among the promising strategies on the horizon. Collaborative efforts between researchers, clinicians and pharmaceutical companies are essential to advance the field and provide better options for individuals living with neurodegenerative diseases.

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## Conflict of Interest

None.

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