

A GUIDE FOR PATIENTS

LITERATURE

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❖ Parkinson's Disease

➤ Mesenchymal Stromal Cell Therapies for Neurodegenerative Diseases

Mesenchymal stromal cells are multipotent cells that are being used to treat a variety of medical conditions. Over the past decade, there has been considerable excitement about using MSCs to treat neurodegenerative diseases, which are diseases that are typically fatal and without other robust therapies. In this review, we discuss the proposed MSC mechanisms of action in neurodegenerative diseases, which include growth factor secretion, exosome secretion, and attenuation of neuroinflammation. We then provide a summary of preclinical and early clinical work on MSC therapies in amyotrophic lateral sclerosis, multiple system atrophy, Parkinson's disease, and Alzheimer's disease. Continued rigorous and controlled studies of MSC therapies will be critical in order to establish efficacy and protect patients from possible untoward side effects.

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➤ Mesenchymal Stem Cells as a Source of Dopaminergic Neurons: A Potential Cell Based Therapy for Parkinson's Disease

Cell repair/replacing strategies for neurodegenerative diseases such as Parkinson's disease depend on well-characterized dopaminergic neuronal candidates that are healthy and show



promising effect on the rejuvenation of degenerated area of the brain. Therefore, it is imperative to develop innovative therapeutic strategies that replace damaged neurons with new/functional dopaminergic neurons. Although several research groups have reported the generation of neural precursors/neurons from human/ mouse embryonic stem cells and mesenchymal stem cells, the latter is considered to be an attractive therapeutic candidate because of its high capacity for self-renewable, no adverse effect to allogeneic versus autologous transplants, high ethical acceptance and no teratoma formation.

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➤ **Cell replacement therapy for Parkinson's disease: how close are we to the clinic?**

Cell replacement therapy (CRT) offers great promise as the future of regenerative medicine in Parkinson's disease (PD). Three decades of experiments have accumulated a wealth of knowledge regarding the replacement of dying neurons by new and healthy dopaminergic neurons transplanted into the brains of animal models and affected patients

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➤ **Role of Mesenchymal Stem Cells in Counteracting Oxidative Stress— Related Neurodegeneration**

Neurodegenerative diseases include a variety of pathologies such as Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and so forth, which share many common characteristics such as oxidative stress, glycation, abnormal protein deposition, inflammation, and progressive neuronal loss. The last century has witnessed significant research to identify mechanisms and risk factors contributing to the complex etiopathogenesis of neurodegenerative diseases, such as genetic, vascular/metabolic, and lifestyle-related factors, which often co-occur and interact with each other. Apart from several environmental or genetic factors, in recent years, much evidence hints that impairment in redox homeostasis is a common mechanism in different neurological diseases.

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➤ **Treatment of Parkinson's Disease through Personalized Medicine and Induced Pluripotent Stem Cells**

Parkinson's Disease (PD) is an intractable disease resulting in localized neurodegeneration of dopaminergic neurons of the substantia nigra pars compacta. Many current therapies of PD can only address the symptoms and not the underlying neurodegeneration of PD. To better understand the pathophysiological condition, researchers continue to seek models that mirror PD's phenotypic manifestations as closely as possible.

Recent advances in the field of cellular reprogramming and personalized medicine now allow for previously unattainable cell therapies and patient-specific modeling of PD using induced pluripotent stem cells (iPSCs). iPSCs can be selectively differentiated into a dopaminergic neuron fate naturally susceptible to neurodegeneration. In iPSC models, unlike other artificially-induced models, endogenous cellular machinery and transcriptional feedback are preserved, a fundamental step in accurately modeling this genetically complex disease.

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➤ Mesenchymal stem cell therapy in Parkinson's disease animal models

Parkinson's disease is a **neurodegenerative disorder** characterized by the loss of **dopaminergic** neurons in the **substantia nigra**, and as a consequence, by decreased dopamine levels in the striatum. Currently available **therapies** are not able to stop or reverse the progression of the disease. A novel therapeutic approach is based on cell therapy with stem cells, in order to replace degenerated neurons. Among stem cells, **mesenchymal stem cells** seemed the most promising thanks to their capacities to differentiate toward **dopaminergic** neurons and to release **neurotrophic factors**.

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➤ **Pluripotent Stem Cell-based therapy for Parkinson's disease: current status and future prospects**

Parkinson's disease (PD) is one of the most common neurodegenerative disorders, which affects about 0.3% of the general population. As the population in the developed world ages, this creates an escalating burden on society both in economic terms and in quality of life for these patients and for the families that support them. Although currently available pharmacological or surgical treatments may significantly improve the quality of life of many patients with PD, these are symptomatic treatments that do not slow or stop the progressive course of the disease. Because motor impairments in PD largely result from loss of midbrain dopamine neurons in the substantia nigra pars compacta, PD has long been considered to be one of the most promising target diseases for cell-based therapy.

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➤ **Stem cell-based approach for the treatment of Parkinson's disease**

Parkinson's disease (PD) is the second most common neurodegenerative brain disorder which is around 1.5 times more common in men than in women. Currently, drug medications, surgery, and lifestyle changes are common approaches to PD, while all of them focused on reducing the symptoms.

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➤ **Stem cell-based therapy for Parkinson's disease**

Motor dysfunctions in Parkinson's disease are considered to be primarily due to the degeneration of dopaminergic neurons in the substantia nigra pars compacta. Pharmacological therapies based on the principle of dopamine replacement are extremely valuable, but suffer from two main drawbacks: troubling side effects (e.g. dyskinesia) and loss of efficacy with disease progression.

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➤ **Stem cell and the treatment of Parkinson's disease**

Progress in Parkinson's disease (PD) research has been hampered by the lack of an appropriate model which exhibits the core pathology seen in the human brain. Recent advances in deriving cells with neuronal phenotypes from patients with neurodegenerative disorders through cellular reprogramming offer a unique tool for disease modelling and may help shed light on the molecular pathogenesis that drives the progression of the disease..

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➤ Stem cell-based therapies for Parkinson's disease

Parkinson disease (PD) is a neurological movement disorder resulting primarily from damage to and degeneration of the nigrostriatal dopaminergic pathway. The pathway consists of neural populations in the substantia nigra that project to the striatum of the brain where they release dopamine. Diagnosis of PD is based on the presence of impaired motor features such as asymmetric or unilateral resting tremor, bradykinesia, and rigidity. Nonmotor features including cognitive impairment, sleep disorders, and autonomic dysfunction are also present.

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