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Research Progress and Future Prospects of Mesenchymal Stem Cell-Derived Exosomes in the Treatment of Neurodegenerative Diseases

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Abstract: Mesenchymal stem cell-derived exosomes carry maternal bioactive components, which are of great significance in promoting tissue and organ development as well as tissue regeneration. In the clinical treatment of neurodegenerative diseases, mesenchymal stem cell-derived exosomes has significant value, can not only promote nerve repair, but also regulate the patient's immune function, which has important value in improving the patient's prognosis. This article will conduct a research review on the basic characteristics of mesenchymal stem cell, combine literature research to study the advantages, biogenesis and composition. This article introduces the research progress of mesenchymal stem cell-derived exosomes in the treatment of neurodegenerative diseases, analyzes the limitations and future prospects, and provides a better reference for clinical treatment.

Keywords: mesenchymal stem cell(MSC)-derived exosomes; neurodegenerative diseases; research progress; future prospects

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1. Introduction

Neurodegenerative diseases(NDDs) are a type of degenerative disease of the nervous system, where patient's neurons and other parts undergo pathological changes, leading to cognitive and speech dysfunction, which affects the patient's normal life[1,2]. Currently, common neurodegenerative diseases in clinical practice include Alzheimer's disease, Huntington's disease, and others. Research has found that mesenchymal stem cell (MSC)-derived exosomes have important clinical application value in NDDs treatment, and have become a key focus of research by scholars both domestically and internationally[3,4]. MSCs are a type of multipotent stem cell with self-renewal ability and the ability to regulate immune function. They have been widely used in the treatment of neurological and cardiovascular diseases[5-6]. MSC-derived exosomes are of great significance in promoting neural repair and improving neurological function in patients, with high safety, and are an important method for clinical treatment of NDDs[7,8]. Overall, in order to better promote the high-quality development of clinical treatment, further understanding of the clinical application of mesenchymal stem cell exosomes is needed, providing scientific guidance for clinical disease treatment.

2. Overview of MSC-derived exosomes

2.1. Basic characteristics of MSCs

MSCs have basic characteristics such as multi-directional differentiation and tissue repair. Adipose tissue, amniotic fluid,

and umbilical cord are important sources of MSCs[9,10]. In clinical treatment, the biological function of MSCs can facilitate the migration of damaged tissues, and further achieve the therapeutic effect of tissue repair. The immunomodulatory function and pluripotent differentiation potential of MSCs make them have broad application prospects in the treatment of NDDs and better promote the development of clinical treatment techniques.

2.2. Biological functions of MSCs

The biological functions of MSCs include multi-directional differentiation, self-renewal, and immune regulation, making them an important method for the clinical treatment of NDDs[11-13]. Firstly, the function of multi-directional differentiation. It can differentiate into various mesenchymal tissue cell lines, such as cardiomyocytes, etc, which can promote vascular tissue recovery, nerve repair, etc. Secondly, self-renewal ability. MSCs can maintain an undifferentiated state and genomic stability while being cultured and expanded in vitro for a long time, and still possess stem cell characteristics even after isolation and expansion. Thirdly, immune regulatory function. MSCs have unique immune regulatory functions, which can release cytokines and inhibit the function of other immune cell subsets.

2.3. Advantages of MSC-derived exosomes

The advantage of MSC-derived exosomes is that they exhibit higher repair ability in clinical treatment, while also ensuring the safety of clinical treatment. MSC-derived exosomes have demonstrated significant clinical advantages in reducing validation reactions, improving neurological function, and promoting neural repair[14,15]. From clinical treatment experience, MSC-derived exosomes are rich in miRNA in the treatment of neurodegenerative diseases. They can reduce cell apoptosis, promote inflammation improvement in patients, and have high clinical treatment safety advantages, reducing the occurrence of immune complications.

2.4. MSC-derived exosomes Biogenesis and Composition

Exosomes are lipid bilayer membrane-bound exosomes composed of lipids, proteins, nucleic acids, and small amounts of metabolites. Exosomes are involved in the pathological processes of various diseases and are also of great significance in intercellular signal transduction. They are rich in various bioactive substances and affect the synthesis and expression of related proteins by regulating the transcription, translation, and expression of receptor cell genes[16,17]. As shown in **Figure 1**, from the perspective of the biogenesis process of exosomes derived from MSCs, the contents of polycystic vesicles can be degraded or released into the extracellular environment. When proteins become targets for lysosomal degradation, polycystic vesicles fuse with lysosomal membranes, leading to the degradation of intracellular vesicles in lysosomes. In addition, polycystic cells can fuse with the plasma membrane and release intracellular vesicles in the form of exosomes from the cell, ultimately generating exosomes[18].

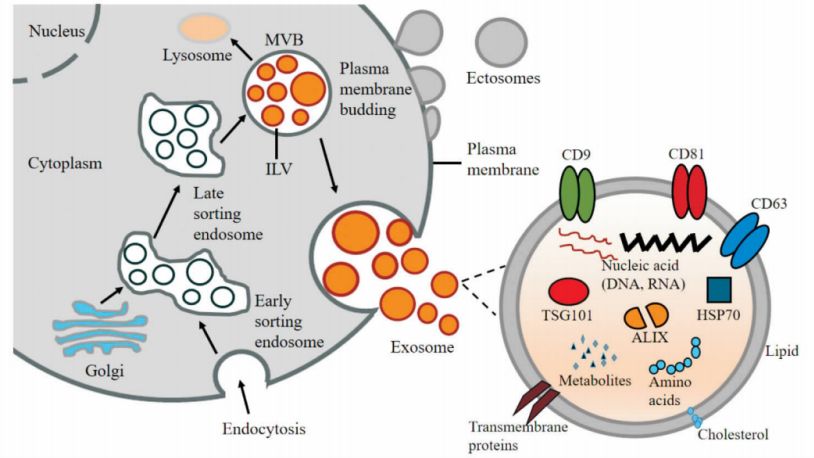

Figure 1. Biogenesis and composition of exosomes[19]

2.5. The mechanism of action of MSC-derived exosomes

In the clinical treatment of NDDs, the mechanism of action of MSC-derived exosomes has immune regulation, promotion of neuronal repair, inhibition of validation cell activation, improvement of brain energy metabolism, et al, to better achieve neuroprotective effects[20-22]. MSC-derived exosomes can activate specific T cell responses, effectively regulate immune responses, and better promote the occurrence of immune responses in patients. At the same time, exosomes from MSCs also have the value of promoting inflammatory responses, which can alleviate nerve damage caused by inflammation and achieve the effect of disease treatment. In terms of promoting neural repair and improving cell apoptosis, MSC-derived exosomes can increase the cell survival rate, promote neuronal repair, and further improve patients' neurological function.

3. Research progress on MSC-derived exosomes for the treatment of neurodegenerative diseases

3.1. Alzheimer's disease

Alzheimer's disease(AD) is a neurodegenerative disease characterized by cognitive impairment, and its main pathogenesis includes neuronal death, pro-inflammatory factors, et al[23]. MSC-derived exosomes are of great significance for the treatment of AD, mainly by promoting anti-inflammatory and nerve cell axon growth, improving patients' immune function, and thus better delaying the occurrence of AD[24]. NAKANO et al[25] pointed out in their study that miR-146a can achieve the value of reducing inflammation, better improving cognitive function, and promoting neurological recovery. SHIN et al[26] pointed out in their study that MSC-derived exosomes have demonstrated superior clinical effects, thereby better achieving the therapeutic effect of Alzheimer's disease cognitive impairment. Overall, they can promote the growth of neuronal axons, thereby better delaying the development of cognitive dysfunction in AD.

3.2. Parkinson's disease

Parkinson's disease(PD) patients are relatively common, and most patients experience symptoms such as neurological dysfunction and bradykinesia. From the perspective of pathogenesis, PD is closely related to mitochondrial damage, neuroinflammation, oxidative stress, and other factors. Multiple studies have shown that MSC-derived exosomes are mainly used in Parkinson's disease treatment by promoting endothelial cell growth, reducing neuronal apoptosis, and promoting the secretion of biomolecules in patients[27,28]. Teixeira et al.[29] found in their study that in Parkinson's disease treatment, MSC-derived exosomes can regulate the dopaminergic system, trigger neural mechanisms, and better achieve therapeutic effects in improving cognitive and motor dysfunction. Xue et al.[30] pointed out in their study, MSC-derived exosomes are of great significance for the generation of endothelial cells in patients. For Parkinson's disease patients, they can increase dopamine levels, better increase cytokine expression, and achieve the effect of relieving cell damage. Overall, in Parkinson's disease treatment, MSC-derived exosomes can affect the activity of target cells, better protect neurological function, and achieve the goal of improving clinical symptoms.

3.3. Spinal Cord Injury

Spinal Cord Injury(SCI) is a neurodegenerative disease with severe trauma, causing local ischemia, edema, et al., which can have adverse effects on the patient's neurological and motor functions, and even lead to complications[31]. MSC-derived exosomes can achieve the goal of inhibiting inflammatory response and reducing cell apoptosis by regulating cytokines in patients, which helps improve neurological function and promote spinal cord cell recovery. Gu et al.[32] found in their study that miRNA-128 can activate autophagy in cells. Not only can it reduce neuronal apoptosis, but it can also achieve the effect of inhibiting cellular inflammation, thereby better promoting the recovery of spinal cord nerve function in patients. Nakazaki et al.[33] point out MSC-derived exosomes can effectively regulate the TGF-β pathway, construct a stable spinal cord microenvironment. Therefore, MSC-derived exosomes can reduce cell apoptosis, promoting neuronal axon generation, improving BSCB and other mechanisms.

3.4. Huntington's Disease

Huntington's disease causes serious harm to the health of patients. Patients may present with symptoms such as dementia, involuntary movement, and mental abnormalities, and even exhibit pathological features of brain tissue atrophy[34]. MSC-derived exosomes promote cell survival in Huntington's disease treatment by inhibiting inflammatory cell activation, reducing neurological dysfunction in patients, and ultimately promoting cell survival[35]. Carmela et al.[36] pointed out in their study that in the treatment of Huntington's disease, MSC-derived exosomes can achieve neuroprotective effects, reduce neuronal damage, better regulate inflammatory cell levels, and thereby improve the neurological dysfunction of Huntington's disease.

3.5. Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a motor neuron degeneration disease. Based on the clinical symptoms of patients, it mainly manifests as muscle weakness, and as the symptoms worsen, it can also cause hemiplegia. From the perspective of pathological mechanisms, impaired RNA metabolism, oxidative stress, and mitochondrial dysfunction are all pathological mechanisms of ALS, which affect the progression of the disease in patients[37]. Debora et al.[38] pointed out in their study that MSC-derived exosomes can improve mitochondrial dysfunction and inhibit cell apoptosis, thereby achieving the treatment of Amyotrophic Lateral Sclerosis. Therefore, in disease treatment, MSC-derived exosomes have good anti-apoptotic effects, and thus better promote the recovery of neuronal cells.

3.6. Multiple Sclerosis

Multiple Sclerosis is commonly found in the brainstem and spinal cord of patients[39]. In clinical practice, many patients may exhibit cognitive and visual impairments. MSC-derived exosomes can improve neuroinflammation, regulate microglial differentiation, and achieve the effect of immunotherapy. In their study, Zhang et al.[40] believed that MSC-derived exosomes have important value in increasing protein levels. By increasing the number of microglia in patients' bodies, they can achieve therapeutic effects in reducing neuroinflammation, better promoting myelin regeneration, and significantly improving patients' cognitive function. Xiao et al.[41] think MSC-derived exosomes can enhance the protective ability of myelin sheaths in clinical treatment, achieve the effect of reducing neuroinflammation in patients, and better promote their health recovery.

4. Challenges and limitations of MSC-derived exosomes in the treatment of ND

MSC-derived exosomes therapeutic efficacy continues to be demonstrated across various experimental models. However, there are still some limitations that affect the high-quality implementation of clinical treatment. Firstly, there are certain limitations in the extraction of exosomes derived from MSCs. The existing techniques for extracting exosomes are relatively outdated and cannot achieve efficient and low-cost extraction, which affects the effectiveness of clinical treatment. Secondly, from the perspective of clinical research, the mechanism of action of exosomes derived from MSC in regulating immune response, promoting neuronal axon generation, and other aspects needs to be further clarified. Existing studies only discuss the important value of exosomes derived from MSCs in these aspects.

In the treatment of ND, MSC-derived exosomes have demonstrated significant therapeutic effects through their diverse biological functions. In order to better promote the high-quality development of clinical therapies based on MSC-derived exosomes, it is essential to actively advance the technology of exosome isolation through the research and development of extracellular vesicle-based drugs, and use biotechnology to improve the efficiency of exosome extraction, thereby improving the clinical treatment effect. In the future, it is necessary to further deepen the research on the mechanism underlying the action of MSC-derived exosomes in the treatment of neurodegenerative diseases, providing scientific guidance for clinical practice.

5. Conclusion

This review article found that MSC-derived exosomes have important clinical value in treating neurodegenerative diseases. They can achieve good clinical therapeutic effects through inhibiting neuroinflammatory responses, promoting vascular cell regeneration, and reducing cell apoptosis.

Disclosure statement

The author declares no conflict of interest.

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