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Mesenchymal stem cells secretions for treating neurological diseases and their mechanism of action

Peng Deng [1,2], Xiangwen Tang [1,2], Hao Yang[1,2]*

1.Shaanxi University of Chinese Medicine, Xianyang 712046, China.
2.Translational Medicine Center, Hong Hui Hospital, Xi'an Jiaotong University, Xi'an 710054, China.

Abstract: Neurological diseases are a class of diseases that seriously affect human health, including stroke, Parkinson's disease, Alzheimer's disease and spinal cord injury. Traditional treatments have some limitations in the treatment of these diseases, such as drug side effects, surgical risks, etc. In recent years, secretions from mesenchymal stem cells (MSCs) have attracted much attention as a new method to treat neurological diseases. The secretions are composed of a variety of bioactive components, which can exert their therapeutic effects by regulating the inflammatory response, promoting the regeneration and repair of nerve cells, and resisting oxidative stress. This review aims to review the application of MSC secretions in the treatment of neurological diseases and explore the mechanism of action.

Keywords: Mesenchymal Stem Cell Secretions; Neurological Diseases; Neuroinflammation; Nerve Repair

1. Introduction

1.1 Background and current status of neurological disorders

Neurological diseases are a large category that contains a wide range of pathological conditions, such as neurodegenerative diseases, stroke, and traumatic brain injury [1]. Globally, neurological diseases have become a major public health problem. The resulting death, disability and socio-economic burden cannot be ignored. Although many traditional treatment modalities exist, new approaches are needed to alleviate the disease process and improve patient quality of life.

1.2 Progress in mesenchymal stem cell secretions

As an important source of mesenchymal stem cells, mesenchymal stem cells (MSCs) have shown promising applications in various tissue repair and disease treatment [2]. Especially in recent years, with the in-depth exploration of MSCs, it was found that a variety of bioactive factors secreted by MSCs show powerful functions in neuroprotection, promoting neuroregeneration, regulating immune response and inhibiting inflammation. Currently, there is extensive research evidence supporting the promising application of MSC secretions in the treatment of neurological diseases [3]. For example, MSC secretions have shown significant effects in the treatment of Parkinson's disease (PD), stroke and traumatic brain injury in experimental animal models. Further studies have found that they mainly achieve neuroprotection through various mechanisms such as inhibiting inflammatory response, and promoting nerve regeneration and cell survival [4-7].

This provides new perspectives and ideas for the application of MSC secretions in the treatment of neurological diseases, and also paves the way for future clinical trials.

2. Components and characteristics of the MSC secretions

2.1 Cytokines and growth factors

MSCs secrete a large number of cytokines and growth factors, such as transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), tumor necrosis factor-α (TNF-α), stem cell factor (SCF) and other [8]. These factors have the function of regulating cell survival, proliferation and differentiation. For example, VEGF stimulates the formation of new blood vessels to provide sufficient nutrients to the damaged nerve tissue; TNF-α regulates the cellular immune response to help resist infection.

2.2 Exosomes and microcysts

MSCs also release small membrane capsules called exosomes and microcapsules. These membrane vesicles contain abundant bioactive molecules such as RNA, protein. Moreover, these molecules may be passed between cells, thus influencing the function of cells [9]. Recent studies showed that exosomes and microcysts secreted by MSCs show important functions in several aspects, including nerve repair and immune regulation.

2.3 Other bioactive molecules

In addition, MSC secretions contain some other types of bioactive molecules, such as antioxidant enzymes, proteases, and their tissue inhibitory factors [9]. These molecules have important roles in maintaining the stability of the tissue microenvironment, regulating cell behavior, and resisting damage. For example, antioxidant enzymes can remove free radicals in the body and protect cells from oxidative stress; proteases and their inhibitory factors are involved in the constant maintenance of the extracellular matrix.

3. MSC secretions in the treatment of neurological disorders

3.1 Stroke treatment

Studies have shown that the application of MSC secretions has great potential for promoting stroke recovery. MSCs can secrete a variety of growth factors and cytokines, which can help to improve the microenvironment and promote the survival and regeneration of nerve cells. Moreover, their secreted exosomes are enriched in miRNA, which can regulate the expression of target genes and further influence neuroprotection and neural repair [10].

3.2 PD treatment

PD is a refractory neurodegenerative disease. However, MSC secretions have shown some therapeutic effects. Some laboratory studies have found that MSCs can reduce symptoms in PD model animals by secreting neuroprotective factors, such as brain-derived neurotrophic factors (BDNF) and catalase, which can effectively protect dopamine neurons from injury [11].

3.3 Alzheimer's disease (AD) treatment

MSCs have also shown some results in the treatment of AD. It has been reported that mesenchymal stem cells can inhibit neuroinflammatory responses and reduce amyloid beta production, which has the potential to improve cognitive function in AD patients [12-15]. Moreover, exosomes secreted by MSC have some effect on nerve regeneration and regeneration.

3.4 Spinal Cord Injury Treatment

MSCs also have significant advantages in managing spinal cord injury [16,17]. The repair effect of MSC is mainly achieved through mechanisms such as inhibiting the inflammatory response, promoting the regeneration of damaged nerve fibers, and stimulating new blood vessel formation. Studies have shown that coronary intravenous injection of MSC or direct transplantation to the site of SCI can significantly improve motor function recovery.

3.5 Treatment for other neurological diseases

In addition to the above diseases, MSCs are also used in the treatment of several other neurological diseases, such as multiple sclerosis, amyotrophic lateral sclerosis, peripheral nerve diseases, and others [18]. Although the treatment of these diseases is experimental, preliminary results show the therapeutic potential of MSC. Overall, MSCs and their secretions provide a new potential therapeutic strategy for neurological diseases through multiple mechanisms of action including anti-inflammatory, immune regulation, as well as promoting the survival and regeneration of nerve cells.

4.Mechanism analysis of mesenchymal stem cell secretions

4.1 Regulate the inflammatory response

MSCs play an important role in regulating inflammatory responses. They can secrete a range of bioactive factors, including but not limited to inflammatory cytokines, growth factors, chemokines, etc., and the interaction between these factors can regulate the inflammatory response of the body. For example, anti-inflammatory cytokines secreted by MSCs such as IL-10 and TGF-β1 can inhibit the neuroinflammatory response to some extent by inhibiting the evolution of T-inducing factors, thereby reducing the damage in neural tissue [19].

4.2 Promote nerve cell regeneration and repair

Treatment with secretions from MSCs is an effective way to promote nerve cell regeneration and repair. MSCs can promote the survival and regeneration of nerve cells by secreting neurotrophic factors and other bioactive components such as BDNF, nerve growth factor, and VEGF [20]. These factors can protect nerve cells and prevent cell apoptosis, while promoting the differentiation of neural stem cells, eventually reaching the goal of repairing the damaged nervous system.

4.3 Anti-oxidative stress

MSCs have significant anti-oxidative stress ability and can effectively resist the oxidative damage of the nervous system caused by various adverse factors. MSCs regulate the redox balance, reduce the damage of free radicals to nerve cells, and protect the normal function of nerve cells. In addition, MSCs can secrete a series of antioxidant enzymes, such as catalase and glutathione, which can remove excessive free radicals in the body and prevent oxidative damage by free radicals to nerve cells [21].

4.4 Progress in studying other mechanisms of action

Exosomes in the secretions of MSCs have attracted much attention recently, and these small RNA and protein-rich vesicles have key roles in cell-to-cell communication. They can affect neuroprotection and nerve repair by regulating gene expression, and can also be released to damaged areas, thus affecting cell behavior, improving cell survival and functional recovery [22]. For example, miRNAs in the exosomes of MSCs are able to regulate the expression of genes involved in neurological diseases to exert a therapeutic effect. Although the research in this field is still in its initial stage, it has shown great potential for application and provided a new research direction for the diagnosis and treatment of neurological diseases.

5. Clinical application prospects and challenges

Although MSCs secretions have shown positive prospects in the treatment of neurological diseases, there are still some challenges in translating them into clinical applications. First, due to the complex composition of MSC secretions, there is no clear standardized production and storage method, which may cause some difficulty in clinical application. Secondly, although preliminary studies have shown the good safety and efficacy of MSC secretions, further verification of these results should be conducted in clinical trials with large samples. Moreover, since the current understanding of the mechanism of action of MSC secretions is incomplete, determining the optimal treatment options suitable for various neurological diseases is also a problem to be solved. Overall, MSC secretion undoubtedly provides new possibilities for the treatment of neurological diseases, but its clinical application still needs more in-depth research and exploration [23].

6. Conclusion

This review summarizes the application of mesenchymal stem cells (MSCs) in the treatment of neurological diseases. As a kind of stem cells with multidirectional differentiation potential, mesenchymal stem cells can secrete a variety of bioactive substances, such as nerve growth factor, BDNF and VEGF, and play anti-inflammatory, antioxidant and anti-apoptotic roles, thereby improving the symptoms of nervous system diseases. The premise of clinical application is the safety of use, so the secretion of mesenchymal stem cells shows a broad development prospect. However, the mechanism of using secretions instead of cell transplantation is still insufficient, and further exploration and

research are still needed to give full play to its therapeutic effect and better serve patients.

References

[1]Xue Xiaoyan, Guo Xiaohua, Li Min, et al. Progress in the pathogenesis of neurodegenerative diseases [J]. Chinese Journal of Gerontology, 2015,35 (11): 3149-3152.

[2] JARMALAVIČIŪTĖ A, PIVORIŪNAS A. Exosomes as a potential novel therapeutic tools against neurodegenerative diseases. Pharmacol Res. 2016;113(Pt B):816-822.

[3] KESHTKAR S, AZARPIRA N, GHAHREMANI MH. Mesenchymal stem cell-derived extracellular vesicles: novel frontiers in regenerative medicine. Stem Cell Res Ther. 2018;9(1):63.

[4] Chen Chen, Huang Hui, Hu Wenjia, Li Xiangyong. Mesenchymal stem cell-derived exosomes for neurodegenerative diseases: problems in application and future prospects [J]. Tissue Engineering Research, China, 2019,23 (9): 1441-1447. DOI:10.3969/j.issn.2095-4344.1582

[5] Lo Furno D, Mannino G , Giuffrida R. Functional role of mesenchymal stem cells in the treatment of chronic neurodegenerative diseases. J Cell Physiol. 2018;233(5): 3982-3999.

[6] GAO ZC, LIU X. The role and application of mesenchymal stem cells-derived exosomes in the treatment of nervous system diseases. Zhongguo Zuzhi Gongcheng Yanjiu. 2020;24(19):3048-3054. DOI:10.3969/j.issn.2095-4344.2040.

[7] SUGAYA K, VAIDYA M. Stem Cell Therapies for Neurodegenerative Diseases. Adv Exp Med Biol. 2018;1056: 61-84.

[8] VIZOSO FJ, EIRO N, CID S, et al. Mesenchymal Stem Cell Secretome: T oward Cell-Free Therapeutic Strategies in Regenerative Medicine. Int J Mol Sci. 2017;18(9):E1852.

[9] DENG H, SUN C, SUN Y , et al. Lipid, Protein, and MicroRNA Composition Within Mesenchymal Stem Cell-Derived Exosomes. Cell Reprogram. 2018;20(3):178-186

[10] ZHANG H, WANG Y , LV Q, et al. MicroRNA-21 Overexpression Promotes the Neuroprotective Efficacy of Mesenchymal Stem Cells for Treatment of Intracerebral Hemorrhage. Front Neurol. 2018;9:931.

[11] Wei Yufan, Fan Feiyan, Li Shuangli, Zhang Yunke. The future of exosomes and mesenchymal stem cells-derived exosomes in the diagnosis and treatment of Parkinson's disease [J]. China Tissue Engineering Research, 2022,26 (25): 4076-4083.

[12] DING M, SHEN Y , WANG P , et al. Exosomes Isolated From Human Umbilical Cord Mesenchymal Stem Cells Alleviate Neuroinflammation and Reduce Amyloid-Beta Deposition by Modulating Microglial Activation in Alzheimer's Disease. Neurochem Res. 2018;43(11):2165-2177.

[13] LIEW LC, KATSUDA T , GAILHOUSTE L, et al. Mesenchymal stem cell-derived extracellular vesicles: a glimmer of hope in treating Alzheimer's disease. Int Immunol. 2017;29(1):11-19.

[14] Golden Saint Yu, Green lett. Progress of mesenchymal stem cell exosomes in the treatment of Alzheimer's disease [J]. Chinese Journal of Cell and Stem Cell: Electronic edition, 2019,9 (4): 247-250

[15] Wang Weili, Song vicissitudes of life. Progress in the pathogenesis of Alzheimer's disease and clinical medication [J]. Drug Evaluation in China, 2019,36 (3): 204-209

[16] Feng Shiqing. Current status and outlook of basic research on spinal cord injury [J]. Chinese Journal of Experimental Surgery, 2021,38 (7): 1193-1198.

[17] LI D, ZHANG P , YAO X, et al. Exosomes Derived From miR-133b-Modified Mesenchymal Stem Cells Promote Recovery After Spinal Cord Injury. Front Neurosci. 2018;12:845.

[18] Zhang Y , Chopp M, Liu XS, et al. Exosomes Derived from Mesenchymal Stromal Cells Promote Axonal Growth of Cortical Neurons. Mol Neurobiol. 2017;54(4):2659-2673.

[19] Chang YH, Wu KC, Harn HJ, et al. Exosomes and Stem Cells in Degenerative Disease Diagnosis and Therapy. Cell Transplant. 2018;27(3):349-363.（

[20] Gao Zhen orange, Liu Xin. Role and application of mesenchymal stem cells in the repair of nervous system diseases [J]. China

Tissue Engineering Research, 2020,24 (19): 3048-3054. DOI:10.3969/j.issn.2095-4344.2040

[21] Ferguson SW, Wang J, Lee CJ, et al. The microRNA regulatory landscape of MSC-derived exosomes: a systems view. Sci Rep. 2018;8(1):1419.

[22] LAI RC, YEO RW, LIM SK. Mesenchymal stem cell exosomes. Semin Cell Dev Biol. 2015;40:82-88

[23] PHINNEY DG , PITTENGER MF . Concise Review: MSC-Derived Exosomes for Cell-Free Therapy. Stem Cells. 2017;35(4):851-858.