Additional comments on extracellular vesicles derived from mesenchymal stem cells mediate extracellular matrix remodeling in osteoarthritis

Pei H et al. Extracellular vesicle therapy for OA
Abstract
Recently, we read an article titled “Extracellular vesicles derived from mesenchymal stem cells mediate extracellular matrix remodeling in osteoarthritis through the transport of microRNA-29a”. The results of this study indicated that engineered exosomes loaded with microRNA-29a (miR-29a) alleviate knee inflammation and maintain extracellular matrix stability in Sprague Dawley rats. The study’s results provide useful information for treating knee osteoarthritis (KOA). This letter, shares our perspectives on treating KOA using engineered exosomes for miR-29a.

Key Words: Exosomes; Intra-articular injection; Mesenchymal stem cells; MicroRNA-29a; Osteoarthritis

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Core Tip: We recently reviewed a study that treated knee osteoarthritis using engineered exosomes. The authors found that this novel treatment approach is more effective than standard exosomes at symptom alleviation. This letter summarizes the advantages and limitations of this therapy and clarifies aspects of the original article.

INTRODUCTION
We recently read an article titled “Extracellular vesicles derived from mesenchymal stem cells mediate extracellular matrix remodeling in osteoarthritis through the transport of microRNA-29a”. In this study, Yang et al[1] used engineered exosomes loaded with microRNA-29a (miR-29a) to treat early knee osteoarthritis (KOA) in rats. The study demonstrated superior pain reduction and joint improvement compared to standard exosomes. It provided a glimmer of hope for novel and exciting approach for
treating KOA without side effects. We hope this piques your curiosity and encourages further exploration of this fascinating topic.

OA is a severe degenerative joint disease characterized by articular cartilage degeneration due to the loss of extracellular matrix, extensive fibrosis, and fissure formation, ultimately leading to the complete loss of the cartilage surface[2]; current first-line drugs for the treatment of OA improve symptoms by suppressing inflammation (using nonsteroidal anti-inflammatory drugs) and lubricating and nourishing the cartilage (using hyaluronic acid); however, these treatments are ineffective at halting cartilage degeneration.

In recent years, the emergence of biologics has provided new insights into the treatment of OA. Our previous studies have identified the excellent potential of platelet-rich plasma and fat microfragments for treating OA[3,4]. Mesenchymal stem cells (MSCs) have garnered significant attention as a promising therapy for delaying or controlling arthritis due to their ability to differentiate into various cell types and their impact on tissue repair and immunomodulation[5]. The paracrine regulatory function of MSCs plays a crucial role in promoting cartilage repair. Jia et al[6] discovered that undifferentiated MSCs were more effective in regenerating hyaline cartilage than in vitro preformed chondrogenic differentiated MSCs. Exosomes, which are secreted by MSCs, have been widely studied for their role in paracrine regulation. Qian et al[7] found that exosomal miR-26b-5p can transform pro-inflammatory M1 macrophages into anti-inflammatory M2 types by targeting the toll-like receptor 3 signaling pathway to alleviate OA. Additionally, Qiu et al[8] found that exosomal miR-485-3p can alleviate cartilage damage in OA by targeting the NR1I1-mediated PI3K/Akt pathway. Furthermore, researchers integrated the less commonly used miR-29a into exosomes, presenting a new approach for treating OA.

CONCLUSION
The use of stem cell exosome miR-29a has produced promising results in reducing the symptoms of OA and promoting cartilage repair and joint function recovery. However,
like any new treatment, certain limitations need to be addressed. For example, the mechanism of action of miR-29a requires further research. Similarly, stem cell exosome preparation and application methods need to be optimized. This highlights the importance of additional research to confirm and build upon the results of the discussed study.
Mingjun Qiu, Yanhua Xie, Guanghua Tan, Xiaoxu Wang, Peiguan Huang, Liang Hong. "Synovial mesenchymal stem cell-derived exosomal miR-485-3p relieves cartilage damage in osteoarthritis by targeting the NRP1-mediated PI3K/Akt pathway", Heliyon, 2024

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