Promising, non-surgical approach to treating rheumatoid arthritis

Exosome Treatment For Rheumatoid Arthritis:

Exosome therapy is a promising, non-surgical approach to treating rheumatoid arthritis (RA) by targeting the root causes of the disease. This therapy works by calming the immune system and stimulating tissue repair, offering a way to reduce inflammation, restore joint function, and improve overall quality of life. Exosomes, derived from stem cells, are nano-sized messengers that can reduce joint inflammation, modulate immune responses, and support the regeneration of damaged tissues. The therapy is currently undergoing clinical research and has shown potential in improving RA symptoms and quality of life for patients.
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Exosomes as Rheumatoid Arthritis Diagnostic Biomarkers and Therapeutic Agents
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Abstract
Rheumatoid arthritis (RA) is a chronic inflammatory joint disorder that causes systemic inflammation, autoimmunity, and joint abnormalities that result in permanent disability. Exosomes are nanosized extracellular particles found in mammals (40–100 nm). They are a transporter of lipids, proteins, and genetic material involved in mammalian cell–cell signaling, biological processes, and cell signaling. Exosomes have been identified as playing a role in rheumatoid arthritis-related joint inflammation (RA). Uniquely functioning extracellular vesicles (EVs) are responsible for the transport of autoantigens and mediators between distant cells. In addition, paracrine factors, such as exosomes, modulate the immunomodulatory function of mesenchymal stem cells (MSCs). In addition to transporting genetic information, exosomes convey miRNAs between cells and have been studied as drug delivery vehicles. In animal models, it has been observed that MSCs secrete EVs with immunomodulatory properties, and promising results have been observed in this area. By understanding the diversity of exosomal contents and their corresponding targets, it may be possible to diagnose autoimmune diseases. Exosomes can be employed as diagnostic biomarkers for immunological disorders. We here discuss

the most recent findings regarding the diagnostic, prognostic, and therapeutic potential of these nanoparticles in rheumatoid arthritis and provide an overview of the evidence pertaining to the biology of exosomes in RA.

The Therapeutic Ability of Exosomes in RA Treatment

MSCs-derived exosomes are an appropriate vector for the transfer of therapeutic miRNA-124a. If this cell was co-incubated with the stated exosome, it induced apoptosis and prevented the migration and proliferation of the FLS cell line. Exosomes are produced from human MSCs that overexpress miRNA-124a. Upon co-incubation with HMSC-124a-EV, these exosomes inhibit the migration and proliferation of FLS cells and enhance their apoptosis [81]. Rheumatoid arthritis fibroblast-like synoviocytes (RA-FLSs) can endocytose exosomes of MSCs with high miR-320a levels. In RA-FLSs, endocytic exosomes release miR-320a, and miR-320a can inhibit CXCL9. CXCL9 promotes RA-FLS invasion and migration by increasing the expression of IL-1, IL-6, and IL-8. A high level of miR-320a expression reduces CXCL9, inhibiting RA-FLS invasion, activation, and migration, and in the CIA model, mice suppress the production of RA and immune factors [80]. According to the analysis of RA patients, angiogenesis and expression of VEGF and MMP14 were raised, whereas expression of miR-150-5p was diminished. It has been discovered that miR-150-5p can influence angiogenesis. It was discovered that miR-150-5p targets and adversely controls VEGF and MMP14 in FLS in a direct manner. Exo-150 suppresses angiogenesis and prevents RA FLS invasion and migration by negatively regulating VEGF and MMP-14. MMPs are associated with synovial inflammation, which destroys articular cartilage. Targeting MMPs could be a potential treatment option for inflammatory joint disorders [79].

Exosomes from stem cell-derived mesenchymal stromal cells are excellent for transferring therapeutic miRNA.

Exosomes derived from human umbilical cord mesenchymal stem cells (hUCMSC-exos) were examined for their beneficial effects on bone destruction in CIA rats. hUCMSC-exos was able to treat bone degeneration in CIA rats without causing any adverse side effects. Therefore, the therapy prevented joint synovial hyperplasia and inhibited the migration of inflammatory cells to the joints. According to their findings, RANKL concentrations decreased in the serum and synovial tissues of CIA rats, whereas OPG concentrations increased. It postulated that an imbalance between RANKL and OPG could be the underlying mechanism for inhibiting bone destruction [86]. MSCs may regulate T cell differentiation and proliferation as well as inhibit proinflammatory factor production. The performance of AT-MSCs derived from human adipose tissue influenced the generation of T regulatory cells (Tregs). They create IL-10 and reduce the immune response, but they inhibit the development of activated $CD4^+$ T cells into T helper (T_H) 17 cells, which produce interleukin (IL)-17 [87]. When the amount of HAND2-AS1 was enhanced in RA FLSs by co-

culturing them with hMSCHAND2-AS1-Exos, the expression of miR-143-3p was inhibited, and the expression of HAND2-AS1 was elevated. HAND2-AS1 was found to increase the expression of TNFAIP3, which is a direct target of miR-143-3p. In RA-FLSs, HAND2-AS1 was discovered to decrease the amount of p-p65, one of the transcription factor families of NF-κB. Consequently, HAND2-AS1 overexpression in exosomes derived from MSCs inhibited progression and induced apoptosis in RA-FLSs by inactivating the NF-κB pathway via the TNFAIP3/miR-143-3p axis [88]. Recent advances in exosome research will disclose the functional pattern and precise properties of exosomes in autoimmune diseases such as RA [89,90]. Exosome-based therapy could provide a safe and new method of treating arthritis. Figure 2 shows in detail how MSC-EVs were used in an experiment for RA treatment and how they affected the immune system. ***Overall, using exosomes to treat arthritis can be regarded as a unique, safe, and adequate therapeutic approach.***

Conclusions

This paper focuses on the therapeutic potential of exosomes. Exosomes convey various molecules, including lipids, RNA, DNA, proteins, and microRNA. Exosomes derived from MSCs have demonstrated the same therapeutic benefits in autoimmune disorders as their origin cells. In addition, mesenchymal-derived exosomes possess immunomodulatory capabilities; however, tailoring these vesicles with anti-inflammatory molecules and specific receptors may enable them to target specific tissues/organs. miRNAs play an important role in determining the therapeutic efficacy of MSC-exosomes in various disorders, and MSC-exosomes are the subject of an expanding body of research. In recent years, a few studies have been undertaken in this field; however, certain challenges remain. Natural carriers, such as exosomes, have advantages and disadvantages compared to synthetic carriers (liposomes or nanoparticles). This includes reduced levels of toxic and immunogenic features, greater stability, longer-lasting maintenance, a low risk of aneuploidy, and a low risk of immunological rejection following in vivo allogeneic injection. The therapeutic potential of exosomes cannot be denied. In addition, several of them can be regarded as valid biomarkers for detecting or even diagnosing RA disease activity. RA, a disease that has resulted in considerable impairment in individuals, has a global influence on people's lives. Several risk variables, including age, smoking, hormones, lifestyle changes, genetics, and epigenetics, are implicated in the pathophysiology of this inflammatory joint disease. Multiple studies have demonstrated the involvement of distinct molecular and cellular signaling pathways in the initiation and progression of RA. A considerable improvement in targeted drug delivery and decreased side effects has been obtained using nanoparticulate technologies. In the future, nanotechnology can potentially improve disease diagnosis, treatment, and research.