

Application of Microvesicles Derived from Stem Cells in Cancer Treatment

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Received March 12, 2024; Accepted March 28, 2024; Online Published March 30, 2024

Dear Editor

Cancer is a significant health issue worldwide, and targeted treatments that can improve survival rates and provide hope for recovery are a priority. Cell therapy is a new approach that uses cells as therapeutic agents. Stem cells have unique biological functions that make them ideal for regenerative medicine, therapeutic carriers, drug targeting, and immune cell production. Mesenchymal stem cells, in particular, have shown promise in clinical trials for treating cancer. Recent studies have revealed that mesenchymal stem cells release extracellular vesicles, tiny particles involved in intercellular communication, programmed cell death regulation, immune response modulation, inflammation, angiogenesis, and coagulation.¹ Extracellular vesicles, such as microvesicles (MVs), have demonstrated significant value as a medical tool. The ability of these nanoparticles to enter cancer cells through the transcytosis and macropinocytosis pathways is one of their most important clinical applications. This allows them to release chemotherapy drugs and increase drug accumulation within cancer cells, leading to more effective treatment outcomes.²

Microvesicles transfer and deliver their contents through specific interactions with ligands and target cell receptors, making them an important tool in the body's physiological and pathological processes, including cell survival, immune regulation, angiogenesis, tissue repair, and regeneration. Mesenchymal stem cell-derived microvesicles contain therapeutic biomolecules

and various paracrine factors that contribute to their therapeutic efficacy, observed in several clinical trials. They are safer and more favorable than MSCs for long-term blood circulation and long-distance therapeutic procedures. They are also helpful in cancer therapy, as they are promising drug delivery systems with high biocompatibility advantages and opportunities for specific targeting and crossing biological barriers.³ They can be precisely targeted by loading drugs or genes into extracellular vesicles such as microvesicles and modifying their surface. Clinical trials have registered mesenchymal stem cell-derived EVs (MSC-EVs) for cancer treatment. Researchers generated MSC-EVs carrying siRNA targeting KRASG12D for metastatic pancreatic cancer treatment. The use of MSC-EVs to deliver KRASG12D inhibitors has the potential for new insights into targeted cancer therapy, ultimately leading to better patient outcomes. MSC-EVs delivering anti-neoplastic drugs could be a promising opportunity for cancer treatment.⁴

Stem cell-derived microvesicles can serve as cell-free therapies and have the advantages of excellent biocompatibility, low immunogenicity, and the ability to cross biological barriers such as the blood-brain barrier (BBB). Vesicles can be genetically modified, making them ideal candidates for the delivery of biological agents. Microvesicles can also be used as cancer vaccines. They have been shown to inhibit tumor growth and cause cell cycle arrest and apoptosis

in vivo. The efficacy of MV tumor vaccines strongly depends on whether they can increase their effectiveness in eliciting an antitumor immune response while limiting their immunosuppressive functions.^{5,6}

Therefore, developing new and targeted treatments that can bring us closer to curing cancer is crucial. Microvesicles are predicted to find applications in the unique place between molecular and cellular medicine and play a role in personalized cancer treatment. However, our fundamental knowledge of their biology is still in the early stages, and much effort must be made to ensure their safe and effective therapeutic use.

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