Commentary

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The Potential Application of Mesenchymal Stem Cell-Derived Extracellular Vesicles Based Therapeutics

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Description

In preclinical human studies, EV-based therapies have been used to treat a variety of organ disorders, but their effectiveness is controversial. On the other hand, many clinical studies have been conducted using recombinant electric vehicles, which are powerful tools for expanding the range of biomedical applications and solving clinical problems.

Application of MSC-EVs in drug delivery

MSCEV is an endogenous vector that reciprocates between cells with excellent biocompatibility. This natural "truck" can transport a variety of bioactive ingredients such as small molecules and drugs. However, the big challenge is loading the cargo into the MSCEV. Previously, cells intended for therapeutic use were designed to overexpress the protein or RNA of interest, but MSCEV packs cargo into MSCEVS by co-culture, electroporation, or sonication. EV expresses targeting peptides encoded by transgenic parent cells on the surface in order to achieve the goal correctly. EV target peptides can facilitate fusion of target cell membranes. This approach can be used to avoid the side effects of chemotherapeutic drugs. In other words, the drug particles can be introduced into MSCEV with antitumor peptides. Therefore, MSCEV not only achieves the right goal, but also enhances its antitumor effect.

Application of MSC-EVs in oncology

Although MSCEV has been shown to be promising in the treatment of tumors, the results are still controversial. For example, secreted MSCEVs, such as MSCs, have immunomodulatory capacity. Dendritic cell (DC) -derived MSCEV is predicted to activate the patient's immune response and eliminate cancer cells. In some preclinical studies, autologous DC-derived MSCEVs trained with tumor antigen peptides *in vitro* showed antitumor potential, but later studies conducted in 2005 showed little therapeutic effect. Therefore, further experiments are needed to optimize MSCEV antitumor applications.

Application of MSC-EVs in hereditary disease

As a natural childbirth tool, EVs may be able to correct mutations associated with hereditary disorders by fusing with recipient cells and transferring biomaterials containing RNA, miRNAs, proteins, and even DNA. Thus, labeled MSCEVs that bind to target cells can mediate the exchange and signal transduction of genetic information. In recent publications, researchers have successfully treated a variety of hereditary genetic disorders with therapeutic MSCEVs.

MSC-EVs modified by engineered biotechnology

For better therapeutic effects, modification of the surface molecules of MSCEV was developed to increase retention in the bloodstream. MSCEV can avoid excretion by the liver, kidney, and reticular endothelial system by altering properties such as particle size, surface receptors, and membrane charge distribution.

Targeted therapy can be achieved by manipulating targeted peptides on the surface of MSCEV to host specific tissues or cells, a process that facilitates more accurate personalized medicine. In 2018, a series of exosome cell transfer (exotic) devices were developed to create bespoke exosomes by constructing mammalian cells using three candidate genes involved in exosome biosynthesis. Exosome production increased more than 15-fold. Therapeutic applications based on RNA delivery will be more convenient by using such devices. In addition, Votteler et al. Designed a self-assembled "envelope protein nanocage" (EPN). Robust EPN biosynthesis contains protein sequence elements encoding three different functions: membrane binding, self-organization, and recruitment of endosome sorting complexes required for efficient transport of cargo to the cytoplasm of recipient cells.

Conclusion

Researchers have also developed bioinspired exosome-mimetic nanovesicles to deliver chemotherapeutic agents to tumor tissue after systemic administration. Exosome- mimetic nanovesicles are produced by degrading monocytes or macrophages by continuous extrusion through filters with smaller pore sizes (10, 5, and 1 μm). These cell-derived nanovesicles have similar properties to exosomes, but with 100-fold higher yields.

In 2019, a new optimized microfluidic cell culture platform called the PDMS Microfluidic Cell Culture Chip was developed. It integrates surface-modified exosome harvesting, antigen modification, and light emission into one workflow. Researchers argued that PDMS microfluidic cell culture chips could easily

harvest intact, engineered antigenic exosomes that could be used to activate antitumor responses.

Together, the progress in engineered MSC-EVs has expedited the translation of stem cell-derived EVs into clinical applications.