PINK1/Parkin Signaling Pathway Plays Pivotal Role in Attenuating Rat Osteoarthritis by BMSC-Derived Extracellular Vesicles

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Abstract

Objective: BMSC-derived extracellular vesicles (BMSC-EVs) have been proved to attenuate osteoarthritis (OA), but the mechanisms are still not very clear. In this study, we explored the role of them in the polarization of macrophages in vitro and the OA rats in vivo. *Methods*: BMSC-EVs were extracted by ultracentrifugation, and identified by transmission electron microscope (TEM), nanoparticle sizer, and western blotting. The mitochondrial membrane damage, production of ROS, and protein expression of Akt, PINK1, and Parkin were determined in vitro. We prepared an OA model of SD rats by resecting the anterior cruciate ligament (ACL) and medial meniscus. Histological analysis and the examination of IL-6, IL-1β, TNF-α, and IL-10 were performed to assess changes in cartilage and synovium. *Results*: BMSC-EVs showed spherical under TEM. The protein markers of CD9, CD81, and TSG101, were observed, and the size distribution of BMSC-EVs was between 50 nm and 120 nm. BMSC-EVs inhibited mitochondrial membrane damage, ROS production, and the protein expression of PINK1 and Parkin. Akt phosphorylation was downregulated under LPS induction, but significantly recovered after adding BMSC-EVs. BMSC-EVs alleviated cartilage injury in OA rats were proved with hematoxylin-eosin (H&E) and safranin-O-fast green staining. According to immunohistochemistry and immunofluorescence analyses, BMSC-EVs inhibited M1 polarization, promoted M2 polarization in the synovium, and decreased the expression of PINK1 and Parkin in the synovium in vivo. The levels of IL-6, IL-1β, TNF-α in the serum were lower, but the level of IL-10 was higher when BMSC-EVs were used in OA rats. *Conclusion*: BMSC-EVs inhibited PINK1/Parkin signaling pathway, which partially regulated synovial macrophage polarization. That might be one of the mechanisms of have been proved to attenuate OA by BMSC-EVs.

Keywords

PINK1/Parkin, BMSC-Derived Exosomes, Osteoarthritis