

# The effects of platelet rich plasma-derived exosome on the osteoarthritic human chondrocytes

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**DISCLOSURES:** None

**INTRODUCTION:** Osteoarthritis (OA) is a degenerative disease that results in the irreversible, progressive destruction of the articular cartilage, causing chronic pain, movement restriction, and eventually reduced quality of life. In spite of fact that the prevalence of OA has steadily increased due to aging, obesity, and sports injuries, placing considerable social burden on public health, promising pharmacological therapy that exhibits convincing disease-modifying efficacy is not discovered yet. As a blood-derived biomaterial, platelet-rich plasma (PRP) has been considered a potential therapy and tried in knee and hip osteoarthritis with beneficial effects as an anti-inflammatory and potent regenerative agent. However, there are some controversial opinions with respect to its efficacy due to the lack of standardization of the PRP preparation procedure. Moreover, PRP is an autologous derivative of whole blood containing various blood-derived cells. Meanwhile, exosomes are small vesicles 50–150 nm in diameter that contain specific proteins, lipids, and nucleic acids, such as DNA, mRNAs, miRNAs, and other non-coding small fragments. Exosomes have been confirmed to have low immunogenicity or tumorigenicity. In this study, we aimed to determine whether PRP-exosome have a promising biological action in the treatment of OA.

**METHODS:** This study was approved by the Public Institutional Review Board of the Ministry of Health and Welfare of South Korea, and written informed consent was obtained from all patients who agreed to participate in this study. Among the patients in our institution who were surgically treated for osteoarthritis of the knee by total knee replacement (TKR) surgery, we selected 37 patients (mean age, 70.3 ± 6.52 years; 9 males and 28 females). Relatively healthy cartilage tissues were obtained by direct dissection following TKR under sterile conditions, and the chondrocytes were isolated from the minced cartilage tissue by type II collagenase digestion method. PRP was prepared by two-step centrifugation of whole blood, and exosome was isolated by exoEasy Maxi Kit (Quiagen). To induce osteoarthritic condition, the primary chondrocytes were treated with 1 ng/ml of IL-1β, and PRP-exosome administration was performed 4 hr after IL-1β challenge for 48 hr. The gene and protein expressions were verified by quantitative real time PCR (qRT-PCR) and Western blot analysis, respectively. Scratch wound assays, cell viability assay and flow cytometric analysis were performed to examine the biological effect of PRP-exosome on the osteoarthritic chondrocytes.

**RESULTS:** In the presence of PRP-exosome, the damaged chondrocytes by IL-1β were dramatically recovered, showing significant cell differentiation and proliferation. PRP-exosome administration led to inverse regulation of the anabolic or catabolic genes for extracellular matrix (ECM) homeostasis in the cartilage which were significantly altered in osteoarthritic condition with IL-1β. Decreased cell population and depleted mitochondrial membrane potential of the damaged chondrocytes by IL-1β were restored with PRP-exosome administration. *Ex vivo* tissue culture revealed that the PRP-exosome-treated chondrocytes have a remarkable adhesive property into a defected cartilage tissue.

**DISCUSSION:** Although we could not identify the potent effector molecule(s) and the molecular mechanisms underlying the regenerative efficacy of PRP-exosome in an inflammatory environment, our study revealed that PRP-exosome has apparent anti-inflammatory, cell proliferative, and regenerative activities in chondrocytes in the presence of IL-1β, which mimic an osteoarthritic environment.

**SIGNIFICANCE/CLINICAL RELEVANCE:** In-depth research of the potential molecular mechanisms and evaluation of the safety for a clinical application of PRP-exosome, it will represent a promising therapeutic approach for OA.

