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The Effect of SIRT1 on NLRP3 (Nucleotide Oligomerization Domain-Like Receptor Family, Pyrin Domain Containing 3) Inflammasome of Osteoarthritis

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Abstract : The role of metabolism in the pathogenesis of osteoarthritis is an emerging field. Metabolic alterations may be a role in osteoarthritis (OA) pathogenesis, and these changes influence joint destruction via several cytokine. Especially, in OA patients, levels of IL-1β are elevated in the synovial fluid, synovial membrane, subchondral bone, and cartilage. The IL-1β is activated by NLRP3 inflammasomes, and NLRP3 inflammasomes are cytosolic complexes that drive the production of other inflammatory cytokines, including IL-1β. In this study, we examined that SIRT1 suppresses IL-1β through inhibiting NLRP3 inflammasomes and SIRT1 ameliorates osteoarthritis. OA fibroblasts were isolated from synovium of OA patients. IL-1β and NLRP3 were detected in synovium of OA patients by immunohistochemistry. Lipopolysaccharides (LPS) stimulated the expression of active IL-1β mRNA in OA fibroblasts and combination of LPS, and adenosine triphosphate increased more the expression of active IL-1β in OA fibroblasts. The level of IL-1β was measured by western blot and ELISA assay. NLRP3 inflammasomes complex were measured by western blot. SIRT1 did not inhibit expression of NLRP3 inflammasome. So caspase-1, apoptotic speck-like protein containing a caspase recruitment domain (ASC) and NLRP3 protein were expressed in OA fibroblasts. But SIRT1 suppressed activation of IL-1β by inhibiting activity of caspase-1 via NLRP3 inflammasome in OA fibroblasts under LPS plus ATP stimulation. These results suggest that SIRT1 is a modulator of NLRP3 inflammasomes in OA fibroblasts and ameliorate IL-1β, so expression of SIRT1 in OA fibroblast may be a potential strategy for OA inflammation treatment.

Keywords : osteoarthritis, inflammasome, SIRT1, IL-1beta
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