Abstract:

We investigated the effects of Tankyrase (TNKS-1/2) inhibitor on mechanical stress-induced gene expressions in human chondrocytes and examined TNKS-1/2 expression in human osteoarthritis (OA) cartilage. Cells were seeded onto stretch chambers and incubated with or without TNKS-1/2 inhibitor (XAV939) for 12 h. Uni-axial cyclic tensile strain (CTS) (0.5 Hz, 8% elongation, 30 min) was applied and the gene expressions of type II collagen a1 chain (*COL2A1*), aggrecan (*ACAN*), SRY-box9 (*SOX9*), *TNKS-1/2*, a disintegrin and metalloproteinase with thrombospondin motifs-5 (*ADAMTS-5*), and matrix metalloproteinase-13 (*MMP-13*) were examined by real-time PCR. The expressions of ADAMTS-5, MMP-13, nuclear translocation of nuclear factor-κB (NF-κB), and β-catenin were examined by immunocytochemistry and western blotting. The concentration of IL-1β in the supernatant was examined by enzyme-linked immunosorbent assay (ELISA). TNKS-1/2 expression was assessed by immunohistochemistry in human OA cartilage obtained at the total knee arthroplasty. *TNKS-1/2* expression was increased after CTS. The expressions of anabolic factors were decreased by CTS, however, these declines were abrogated by XAV939. XAV939 suppressed CTS-induced expressions of catabolic factors, release of IL-1β as well as nuclear translocation of NF-κB and β-catenin. TNKS-1/2 expression increased in mild and moderate OA cartilage. Our results demonstrated that XAV939 suppressed mechanical stress-induced expressions of catabolic proteases by inhibition of NF-κB and β-catenin-activation, indicating TNKS-1/2 expression might be associated with OA pathogenesis.