Transferrin receptor-1

Transferrin receptor-1 (TfR1) plays important roles in controlling cellular iron levels, but its role in osteoarthritis pathology is unknown. Wang et al. aim to investigate the role of TfR1 in OA progression and its underlying mechanisms.

TfR1 expression in cartilage during OA development were examined both in vivo and in vitro. Then IL-1β was used to induce chondrocytes degeneration in vitro and TfR1 siRNA was used for observing the effect of TfR1 in modulating iron homeostasis, mitochondrial function and degrading enzymes expression. Also the inhibitor of TfR1 was exploited to analyze the protective effect of TfR1 inhibition in vivo.

TfR1 is elevated in OA cartilage and contributes to OA inflammation condition. Excess iron not only results in oxidative stress damage and sensitizes chondrocytes to ferroptosis, but also triggers c-GAS/STING-mediated inflammation by promoting mitochondrial destruction and the release of mtDNA. Silencing TfR1 using TfR1 siRNA not only reduced iron content in chondrocytes and inhibited oxidative stress, but also facilitated the mitophagy process and suppressed mtDNA/cGAS/STING-mediated inflammation. Importantly, we also found that Ferstatin II, a novel and selective TfR1 inhibitor, could substantially suppress TfR1 activity both in vivo and in vitro and ameliorated cartilage degeneration.

The work demonstrates that TfR1 mediated iron influx plays important roles in chondrocytes degeneration and OA pathogenesis, suggesting that maintaining iron homeostasis through the targeting of TfR1 may represent a novel therapeutic strategy for the treatment of OA [1)]

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Wang W, Ma Z, Feng X, Ren J, Sun S, Shao Y, Zhang W, Yang X, Zhang J, Jing X. TfR1 mediated iron metabolism dysfunction as a potential therapeutic target for osteoarthritis. Arthritis Res Ther. 2024 Mar 16;26(1):71. doi: 10.1186/s13075-024-03304-x. PMID: 38493104.