KLF15 affects the progression of arthropathy in inflammatory arthritis

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INTRODUCTION: Kruppel-like zinc finger transcription factor 15 (KLF 15) is a transcription factor that regulates physiological systems. It is also reported that KLF15 regulates adipocyte differentiation via PPARγ, and PPARγ suppresses joint inflammation via the NFk-β pathway. The purpose of this study was to clarify the effects of KLF15 in a mouse Collagen Antibody Induced Arthritis (CAIA) model.

METHODS: Tamoxifen-induced cartilage-specific KLF15 knockout (KO) mice were generated and tamoxifen was administered intraperitoneally for 5 consecutive days at 6 weeks of age. An anti-type II collagen monoclonal antibody was intraperitoneally administered to 10-week-old male KO mice (KO group) and wild-type mice (WT group). On the 3rd day after administration, Lipopolysaccharide (LPS) was additionally administered to create a mouse CAIA model. In both groups, the knee joints were collected at 0, 1, 2, and 4 weeks after antibody administration, and were evaluated histologically (safranin-O, HE), immunohistologically (PPARγ, pIKK α/β, IL-1β, MMP3, MMP-13) were evaluated and compared between the two groups.

RESULTS: The arthropathy score was significantly higher in the KO group at 4 weeks, and the synovitis score did not differ significantly at each time point (Figure.1). At each time point, PPARγ decreased significantly in the KO group (Figure.2), and pIKK α/β, IL-1β, MMP-3, and MMP-13 increased significantly in the KO group (Figure.3).

DISCUSSION: Induction of arthritis in cartilage-specific KLF15KO mice increased inflammatory markers and matrix-degrading enzymes in cartilage and suppressed cartilage degeneration. Decreased anti-inflammatory PPAR-γ expression in articular cartilage increased its downstream pIKK α/β. As a result, it was possible that IL-1β, MMP-3, 13 expression was significantly increased locally in the articular cartilage.

SIGNIFICANCE/CLINICAL RELEVANCE: The results suggested that testing KLF15 as an inflammatory arthritis therapeutic should be a focus in further research.


Figures:

Figure 1

Figure 2

Figure 3

ORS 2024 Annual Meeting Paper No. 1541