Type II collagen peptide Coll2-1 is an actor of synovitis

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Summary

Objective

We evaluated the ability of Coll2-1, a type II collagen peptide, to activate pro-inflammatory pathways in synovial cells and to induce arthritis in Lewis rats.

Method

Human synoviocytes and chondrocytes from knee OA patients were cultured for 24 h with/without Coll2-1 and/or purified immunoglobulin G (AS0619) binding specifically this peptide, and/or CLI-095, a TLR-4 signaling inhibitor and/or apocynin and diphenyleneiodonium, Reactive oxygen species (ROS) production inhibitors. The Interleukin (IL)-8 and Vascular Endothelium Growth Factor (VEGF) expression, the IL-8 production, the IκB-α and p65 phosphorylation and ROS were evaluated. Coll2-1 peptide, bovine type II collagen (CIA), streptococcal cell wall (SCW) or saline solution were injected into Lewis rats. The Coll2-1 peptide was injected subcutaneously (SC; 20–200μg/100μl/animal) or intra-articularly (IA; 0.5–5μg/50μl/animal) and compared to CIA injected in SC (200μg/100μl/animal) and SCW in IA (5μg/50μl/animal). The animals were injected on day 0 and monitored for 28 days. Histological lesions assessment was performed using an arthritis score.

Results

Coll2-1 peptide significantly increased IL-8 gene expression and production by synoviocytes. AS0619 and CLI-095 significantly decreased IL-8 expression. Coll2-1 induced p65 and IκBα phosphorylation and oxidative stress inhibitors decreased it. In human chondrocytes culture, Coll2-1 significantly increased MMP-3 and VEGF gene expression. In Lewis rats, CIA, SCW or Coll2-1 injection triggered arthritis. Like CIA or SCW, Coll2-1 induced synovitis, loss of cartilage proteoglycans, cartilage structure lesion and subchondral bone remodeling.

Conclusions

Coll2-1 activates synoviocytes to produce IL-8 and induces arthritis in rat. These findings suggest that neutralizing Coll2-1 could be a therapeutic approach of arthritis.

Keywords:
Synovitis, Inflammation, Coll2-1 peptide, Matrix biotherapy