Abstract

Dysregulation between pro- and anti-inflammatory cytokines activity in rheumatoid arthritis (RA) contributes to immune dysregulation, chronic inflammation and subsequent joint destruction. Interleukin-37 (IL-37) has been described as an anti-inflammatory cytokine in several autoimmune diseases.

The main aim of this work was to determine the levels of IL-37 in serum and synovial fluid (SF) of RA patients and to compare them with the levels in patients with osteoarthritis (OA) and further explore the association of IL-37 with disease activity and other clinical parameters. Subsequent goal was to study its anti-inflammatory function on RA synovial fibroblasts and describe other cells types of synovial tissue contributing to its production.

IL-37 levels were detected using enzyme-linked immunosorbent assay (ELISA). Synovial fibroblasts were stimulated by lipopolysaccharide (LPS) and recombinant IL-37 (rIL-37). The levels of studied genes were detected by PCR. Synovial tissues and immune cells were visualized by immunohistochemical and by immunofluorescence staining.

We found increased levels of IL-37 in SF of patients with RA in comparison to OA patients. There was a significant correlation between serum and SF levels of IL-37. RA as well as OA patients showed increased levels of IL-37 in serum than in SF. Levels of IL-37 in SF positively correlated with levels of CRP. Serum levels of IL-37 showed negative correlation with HDL levels and positive correlation with atherogenic index. LPS induced RA synovial fibroblasts exhibited lower expression of pro-inflammatory cytokines upon stimulation with IL-37. IL-37 was produced by macrophages, synovial fibroblasts and T- and B-lymphocytes of synovial tissue.

Results of our study showed a significant anti-inflammatory role of IL-37 in RA. These findings may have a potential translational implication as new therapeutic targets are essential for the successful treatment of inflammatory diseases.

Keywords: interleukin-37, rheumatoid arthritis, autoimmune disease, anti-inflammatory cytokine