

## Interleukin-18 expression in rheumatoid artheritis synovial tissue and its relation to disease activity

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The study investigates the expression and function of interleukin-18 (IL-18) in synovial tissue (ST) of patients with rheumatoid arthritis (RA). IL-18 and IL-18 receptors (IL-18R) mRNA expression was detected by reverse transcription-polymerase chain reaction (RT-PCR). Expression of IL-18 at protein level was analyzed by western blotting technique. Cytokines; (IL-18 and interferon-[IFN-gamma]) in culture supernatants from ST cell organ and synovial cultures and IL-18 in sera and synovial fluid (SF) were measured by ELISA. The ST samples were taken from 44 RA patients and thirty osteoarthritis patients (OA) were included as controls. Using RT-PCR, for ST of RA and OA, mRNA expression of IL-18 was detected in 39 out of 44 (88.6%) RA patients and in 14 out of 30 (46.6%) OA controls. However, mRNA expression of IL-18 R alpha and beta chains were detected in 39 and 35 out of 44 (88.6% and 79.5%) RA patients, respectively. ST of OA did not express mRNA of alpha and beta chains of IL-18 R. In vitro study of IL-18 production by ST showed significantly higher levels in RA compared to that of OA patients ( $P < 0.005$ ). Western blotting revealed that the expression of ST IL-18 was more in RA than in OA ( $P < 0.02$ ). Only IL-12, but not IL-18, stimulates IFN-gamma production by RAST cells [mean  $\pm$  SD = 246  $\pm$  15 pg/ml]. However, when IL-12 was combined with IL-18, they could significantly stimulate IFN-gamma production by RAST cells [M  $\pm$  SD = 629  $\pm$  18 pg/ml]. OA ST cells did not respond to either IL-12 alone or when combined to IL-18. IL-18 was detected at significantly higher levels in sera and SF of RA patients in comparison to OA controls ( $p < 0.001$  and  $p < 0.01$ , respectively). IL-18 level in the sera and SF in RA patients was significantly correlated with disease activity. In conclusion, IL-18 is expressed in RA synovia and contributes to the production of IFN-gamma by the infiltrating T-cells. These cytokines could play a proinflammatory role in the pathogenesis of RA.