Interleukin-37 attenuates the inflammatory response in patients with Rheumatoid arthritis and ameliorates collagen-induced arthritis via suppressing Th17 related cytokine production

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Interleukin (IL)-37 is a natural inhibitor of innate immunity associated with several autoimmune diseases. High levels of IL-37 are expressed in serum and synovium of patients with Rheumatoid arthritis (RA) suggesting a potential role of IL-37 in RA. This study was undertaken to evaluate whether IL-37 has anti-arthritic effects. We demonstrated RA patients with active disease showed higher IL-37 mRNA and serum protein levels as compared with those with inactive disease as well as healthy controls. Serum IL-37 levels correlated with Th17 related cytokines. Compared with healthy controls, IL-37 mRNA was up-regulated in CD3+ T cells and CD4+ T cells of patients with RA. Furthermore, Th1 and Th17 differentiation noticeably enhanced IL-37 expression. HrIL-37 reduced Th17 related cytokine expression and Th17 cells proportion in PBMCs and purified CD4+ T cells from patients with RA. Mice injected with Ad-IL-37 showed attenuated severity of arthritis based on clinical scores and paw swelling. Histological analysis of arthritic joints from Ad-IL-37-treated mice demonstrated significant diminution of synovial hyperplasia and joint damage. IL-17 and cytokines inducing Th17 cells differentiation as well as IL-17 downstream targets gene expressions were markedly reduced in synovium from CIA mice receiving injection of Ad-IL-37. Moreover, hrIL-37 down-regulated Th17 associated genes expression in joint cells from arthritic mice in vitro. Obtained findings indicate that IL-37 associated with RA disease activity as well as Th17 related cytokines and plays a potent immunosuppressive role in the pathogenesis of both human RA and CIA models by down-regulating Th17 associated pro-inflammatory cytokines and IL-17 downstream targets genes.

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