expressed on osteoclast precursor, providing the signals necessary for osteoclast differentiation [Suda et al., 1999]. A combination of IL-6 and soluble IL-6 receptor reportedly induces RANKL expression in UAMS-32 stromal/osteoblastic cell line [O'Brien et al., 1999]. In has been reported that RANK expression is markedly increased by TNF-α in bone marrow cells containing osteoclast precursors [Komine et al., 2001]. Furthermore, it has recently been reported that overexpression of IL-17 promotes RANKL and RANK expression in synovium, resulting in increase of osteoclastic bone resorption and bone erosion in collagen-induced arthritis [Lubberts et al., 2003]. Taking these findings into account, it is likely that the enhancement by IL-17 of TNF-α-induced IL-6 synthesis in osteoblasts acts as a potent positive regulating mechanism of osteoclastic bone resorption cooperatively with RANKL/RANK pathway in the inflammatory bone resorption. Further in vivo and ex vivo investigations using osteoprotegerin, a decoy receptor of RANK which blocks the RANKL signals to osteoclast, or the antibodies for RANKL would be required to clarify the exact mechanism of pathological bone resorption in inflammatory bone diseases.

In conclusion, our present results strongly suggest that IL-17 stimulates TNF-α-induced IL-6 synthesis via p38 MAP kinase activation in osteoblasts.

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